EC6191

PRACTICE OF MEDICINE

VOLUME VI

PRACTICE OF MEDICINE

EDITED BY

FREDERICK TICE, M.D.

PROFESSOR OF MEDICINE AND CLINICAL MEDICINE, AND
HEAD OF THE DEPARTMENT OF MEDICINE,
UNIVERSITY OF ILLINOIS, COLLEGE
OF MEDICINE

FOREWORD BY

M. W. IRELAND, M.D.

SURGEON-GENERAL, U. S. ARMY

VOLUME VI

HAGERSTOWN, MARYLAND
W. F. PRIOR COMPANY, INC.
1924

Copyright, 1924 by
W. F. PRIOR COMPANY, INC.

Printed in the United States of America

CONTENTS

VOLUME VI

SECTION IV: DISEASES OF THE CIRCULATORY SYSTEM

CHAPTER PAGE

I. DISEASES OF THE ARTERIES AND CLINICAL BLOOD-PRESSURE 1

By Louis M. Warfield

Arteriosclerosis 2
  General Definition and Etiology 2
  General Anatomy of the Arteries 2
  Physiology of the Arteries 4
  Etiology 5
    Causative Factor 5
      Congenital 6
      Acquired 6
  Symptomatology 7
    General Symptoms 7
    Hypertension 8
    Angina Abdominalis 9
    Thrombosis of Mesenteric Arteries 9
  Diagnosis 10
  Complications 11
  Association with Other Diseases 11
  Treatment 12
  Prognosis 12
  Pathology 13
Thrombo-angiitis Obliterans 15
  Definition 15
  Etiology 15
  Symptomatology 16
  Diagnosis 17
  Complications and Sequelæ 17
  Treatment 17
  Prognosis 17
  Pathology 17
    Healed Stage 18
    Acute or Specific Lesion 18
Syphilitic Arteriosclerosis (Arteritis) 18
Syphilitic Aortitis 19
  Definition 19
  Etiology 19
  Symptomatology 19
    Physical Findings 20

PAGE
- Diagnosis . . . 21
- Treatment . . . 22
- Pathology . . . 22

Aneurysm . . . 23
- Definition . . . 23
  - True Aneurysm . . . 23
  - Sacculated Aneurysm . . . 23
  - Fusiform Aneurysm . . . 24
  - Dissecting Aneurysm . . . 24
  - False Aneurysm . . . 24
  - Arteriovenous Aneurysm . . . 24
  - Cirsoid Aneurysm . . . 24
- Etiology . . . 24
- Symptomatology . . . 26
  - Physical Findings . . . 29
  - Development of Aneurysm . . . 31
  - Rupture . . . 31
- Diagnosis . . . 32
- Clinical Varieties . . . 32
  - Dissecting Aneurysm . . . 32
  - Arteriovenous Aneurysm . . . 32
  - Aneurysm of Abdominal Aorta . . . 33
  - Aneurysms of Other Varieties . . . 34
- Treatment . . . 34
- Prognosis . . . 35
- Pathology . . . 36
- Historical Summary . . . 36

Thrombosis of the Coronary Arteries . . . 36
- Definition . . . 36
- Etiology . . . 36
- Symptomatology . . . 37
- Diagnosis . . . 37
- Complications . . . 38
- Clinical Varieties . . . 38
- Treatment . . . 38
- Prognosis . . . 38
- Pathology . . . 39

Periarteritis Nodosa . . . 40
- Definition . . . 40
- Etiology . . . 40
- Symptomatology . . . 40
- Diagnosis . . . 40
- Treatment . . . 41
- Prognosis . . . 41
- Pathology . . . 41

Clinical Blood-pressure . . . 41
- Definition . . . 41
- Technic of Blood-pressure Measurements . . . 42
- Mechanism of Maintenance of Blood-pressure . . . 43
  - Vasomotor System . . . 44
  - Effects of Chemical Substances . . . 45
  - Respiratory Effects . . . 45
- Average Normal Blood-pressure . . . 46
  - Variations in Blood-pressure Under Physiological Conditions 47
  - Pressure in Different Branches of Vascular Tree . . . 48
- Functional Tests in Relation to Blood-pressure . . . 49
- Hypotension . . . 52
- Hypertension . . . 53
  - Etiology . . . 53

CHAPTER PAGE
Clinical Varieties 54
Treatment 60
Prognosis 61
Occurrence in Various Conditions 62
Blood-pressure in Acute Infections 62
Blood-pressure in Chronic Infections 62
Blood-pressure in Surgical Conditions 62
Blood-pressure in Obstetrics 64
Blood-pressure in Blood Diseases 64
Blood-pressure in Cardiac Diseases 64
Value of Blood-pressure Estimations 65

II. ACUTE ENDOCARDITIS 67
By Henry G. Webster
Definition 67
Etiology 68
Exciting Cause 68
Pathology 69
Dynamic Factors 70
Simple Acute Endocarditis 71
Etiology 71
Symptomatology 71
Evanescent Type 71
Well-defined Type 72
Course of Disease 73
Complications 74
Treatment of Acute Endocarditis 75
Prognosis of Simple Endocarditis 77
Sociological Aspect 78
Malignant Endocarditis 78
Clinical Varieties 79
Pyemic Form 79
Typhoid Form 80
Cardiac or Recurrent Form 81
Afebrile Form 81
Cerebral Form 81
Chronic Septic Endocarditis 81
Differential Diagnosis of Malignant Endocarditis 84
Typhoid Fever 84
Rheumatic Fever 84
Malaria 84
Miliary Tuberculosis 84
Pneumonia 84
Spinal Meningitis 84
Exophthalmic Goiter 84
Treatment of Malignant Endocarditis 85
General Management 85
Hypodermatic Treatment 85
Prophylaxis 86
Medicinal Treatment 86
Prognosis 87
Occurrence and Distribution 87
Identification of Murmurs 87
Mitral Regurgitation (Mitral Insufficiency or Incompetency) . 87
Mitral Stenosis 88
Aortic Regurgitation (Aortic Insufficiency or Incompetency) . 88
Aortic Stenosis 89
Tricuspid Regurgitation (Insufficiency or Incompetency) . . 89

CHAPTER PAGE
III. CHRONIC VALVULAR DISEASE OF THE HEART . . . 91
By Thomas F. Reilly
Introduction . . . 91
Aortic Stenosis . . . 93
  Etiology . . . 93
  Symptomatology . . . 93
    Physical Signs . . . 94
    Special Examinations . . . 95
  Diagnosis . . . 96
  Prognosis . . . 97
  Pathology . . . 98
Aortic Insufficiency (Aortic Regurgitation) . . . 99
  Etiology . . . 99
  Symptomatology . . . 100
    Physical Findings . . . 102
    Flint Murmur . . . 105
    Evidences of Aortic Regurgitation Outside the Heart . . . 105
    Special Examinations . . . 106
  Diagnosis . . . 106
    Differential Diagnosis . . . 107
  Treatment . . . 107
  Prognosis . . . 109
  Pathology and Pathological Physiology . . . 111
Mitral Regurgitation . . . 112
  Etiology . . . 112
  Symptomatology . . . 113
    General Symptoms . . . 113
    Kidneys . . . 117
    Physical Findings . . . 118
    Special Examination . . . 120
  Diagnosis . . . 120
  Prognosis . . . 123
  Pathology . . . 126
Mitral Stenosis . . . 127
  Etiology . . . 127
  Symptomatology . . . 128
    Clinical History . . . 128
    Physical Findings . . . 130
    Special Findings . . . 133
  Diagnosis . . . 134
  Complications and Sequelæ . . . 139
  Prognosis . . . 141
  Pathology and Pathological Physiology . . . 144
Tricuspid Regurgitation . . . 146
  Etiology . . . 146
  Symptomatology . . . 147
  Differential Diagnosis . . . 148
  Prognosis . . . 148
  Pathology and Pathological Physiology . . . 149
Tricuspid Stenosis . . . 149
  Etiology . . . 149
  Symptomatology . . . 149
  Diagnosis . . . 149
    Physical Signs . . . 149
    Differential Diagnosis . . . 150
  Prognosis . . . 150
  Pathology and Pathological Physiology . . . 151

CHAPTER PAGE
Pulmonary Stenosis 151
  Etiology 151
  Symptomatology 151
  Diagnosis 152
  Prognosis 152
  Pathology and Pathological Physiology 152
Pulmonary Regurgitation 152
  Etiology 152
  Symptomatology 153
  Differential Diagnosis 153
  Prognosis 153
  Pathology and Pathological Physiology 154
General Prognosis of Chronic Valvular Disease 154
  Cause of Cardiac Lesion 156
    Recurring "Rheumatic Carditis" 156
    Rheumatic Fever 156
    Syphilitic Cases 157
    Arteriosclerotic Form 157
  Kind of a Person Who Has Heart Disease 158
    Heredity 158
    Occupation 159
    Climate 159
    Age 159
  Conditions Affecting the Prognosis 160
    Murmur 160
    Combined Lesion 160
General Treatment of Valvular Disease 164
  Cases Discovered by Accident and Presenting No Symptoms . 164
  Outline of Treatment of a Case of Valvular Disease (When Discovered by Accident with or without the History of Previous Loss of Compensation) 166
  Cases Presenting Minor Symptoms Which Accompany Valvular Disease 166
    Special Indications 167
Outline of Treatment when Minor Symptoms Have Appeared . 171
Individual Symptoms and Their Treatment 172
Broken Compensation 183
  Diet 184
  Hope 185
  Digitalis 185
  Opium 191
  Other Drugs of Use in Cardiac Diseases 192
  Therapeutic Measures Other Than Drugs 195
Outline of Treatment for Patient Suffering from One or More of the Marked Symptoms of Decompensation . . . 200

IV. DISEASES OF THE PERICARDIUM 205

By Frederick Tice

Pericarditis 205
  Definition 205
  Etiology 206
  Bacteriology 208
  Clinical Varieties 208
  Acute Plastic Pericarditis 208
  Pericarditis with Effusion 210

CHAPTER PAGE
Pericarditis Sicca 216
Serofibrinous Pericarditis 216
Purulent Pericarditis 216
Hemorrhagic Pericarditis 216
Tuberculous Pericarditis 217
Luetic Pericarditis 217
Chronic Pericarditis 217
Adherent Pericardium 224
Hydropericardium 234
Hemopericardium 235
Pneumopericardium 237
Neoplasms of the Pericardium 240
History 241
Bibliography 242

V. ANGINA PECTORIS 253

BY ALEXANDER LAMBERT

Definition 253
Etiology 253
Symptomatology 259
Diagnosis 259
Complication and sequelae 267
Association with other diseases 267
Clinical varieties 267
Angina sine dolore 268
Pseudo-angina 269
Toxic anginas 269
Abdominal anginas 271
Treatment 272
Prognosis 276
Pathology 277
Historical summary 278

VI. INSTRUMENTS OF PRECISION IN CARDIOVASCULAR STUDIES 281

BY ALEXANDER LAMBERT

Historical 281
Instruments 289
Stethoscope 289
Phonendoscope 291
Sphygmograph and Electrocardiograph 291
Physiology of the cardiac cycle 294
Cardiographic curves 295
Methods of taking tracings 299
Reading of tracings 300
Measuring of tracings 303
Significance of various curves 304
Cardiac arrhythmias 305
Auricular irreglarities 305
Heart Block 308
Ventricular ectopic beats 309

CHAPTER PAGE
Pulsus alternans 309
Crehore micrographic curves 309
Jacquet curves 310
Electrocardiograms 312
Method of making electrocardiograms 313
Interpreting electrocardiograms 313
Curves taken with the optical capsule of Franck 318

VII. MYCOCARDITIS 319

By Alexander Lambert

Definition 319
Etiology 319
Symptomatology 322
Acute myocarditis 330
Chronic myocarditis 332
Sinus arrhythmia 338
Extrasystoles 339
Paroxysmal tachycardia 340
Auricular flutter 341
Auricular fibrillation 342
Heart block 343
Stokes-Adams syndrome 345
Pulsus alternans 346
Ventricular fibrillation 346
Diagnosis 347
Complications and sequelae 349
Association with other diseases 349
Diphtheria 349
Rheumatism 350
Syphilis 351
Influenza 351
Neuroses 351
Fatty Heart 355
Clinical variations 356
Treatment 359
Acute myocarditis 359
Chronic myocarditis 360
Prognosis 372
Pathology 375

SECTION V: DISEASES DUE TO PHYSICAL AGENTS.

I. HEAT EXHAUSTION 381

By L. C. Johnson

Definition 381
Etiology 381
Exciting causes 385
Symptomatology 385
Clinical History 385
Physical findings 386

CHAPTER PAGE
Laboratory findings 387
Diagnosis 387
Complications 387
Treatment 389
Prophylaxis 389
General management 389
Management of convalescence 390
Prognosis 391
Pathology 391
Historical Summary 392

II. MORBID CONDITIONS DUE TO CHANGES IN BAROMETRIC PRESSURE 395

By Joseph W. Schereschewsky

Introduction 395
Conditions due to compressed air 395
Work in compressed air 395
Physical laws to which compressed air workers are subject 397
Respiratory requirements of the body at atmospheric pressure 397
Law of partial pressure 398
Volume of air required in compressed air work 398
Description of compressed air illness 402
Cause of compressed air illness 407
Prevention of compressed air illness 411
Treatment of compressed air illness 423
Devices for safety and comfort of workers 425
Conditions due to diminished barometric pressure 426
Symptoms of mountain sickness 427
Types of mountain sickness 428
Cause of mountain sickness 430
Prevention of mountain sickness 443
Bibliography 444

SECTION VI: DISEASES OF THE BONES AND JOINTS

I. DISEASES OF THE BONES AND JOINTS 449

By Robert Soutter

Diseases of the Bones 450
Fractures 450
Fracture of the Spine 450
Fracture of the Neck of the Femur 451
Fracture of the Metatarsal Bones 451
Tibial Tubercle Injury or Separation 451
Absence of Bones 452
Congenital Absence of the Long Bone—Absence of the Fibula 452
Congenital Absence or Partial Absence of Other Long Bones 453
Absence and Malformation of Vertebræ 454
Absence of Ribs 454
Deformities 455
Deformity of the Thorax 455

CHAPTER PAGE
- Supernumerary Ribs—Absence of Ribs 455
- Deformity of Chest from Rickets 455
- Funnel Chest 455
- Pigeon Breast 455
- Deformity of the Spine 456
  - Round Shoulders—Stoop Shoulders 456
  - Scoliosis 457
  - Spina Bifida Occulta 458
- Deformity of the Toes 459
  - Claw-foot and Hammer-toes 459
- Deformities of the Fingers 460
  - Webbed Finger 460
  - Hypertrophic Osteo-Arthropathy 461
  - Distorted Fingers 461
- Other Deformities 461
  - Congenital Elevation of the Scapula—Sprengel's Deformity 461
  - Bow-legs and Knock-knees 462
  - Acromegaly 463
  - Achondroplasia — (Chondrodystrophia) — Achondroplasia Fetalis 465
- Tuberculosis and Other Diseases of the Bones 465
  - Tuberculosis of the Bones and Joints 465
- Tuberculosis of the Spine (Pott's Disease) 469
- Periostitis 476
- Osteomyelitis 477
- Typhoid Spine 479
- Infantile Paralysis 479
- Non-infectious Paralyses 482
  - Cerebral Spastic Paralysis 482
  - Spastic Spinal Paralysis 483
  - Obstetrical Paralysis 484
- Other Pathological Conditions of the Bones 484
  - Progressive Muscular Atrophy 484
  - Infantile Scurvy 485
  - Congenital Torticollis 485
  - Acquired Torticollis 486
  - Sciatic Scoliosis 487
  - Back-strain 487
  - Osteogenesis Imperfecta—Fragilitas Ossium 488
  - Osteomalacia 488
  - Osteitis Deformans (Paget's Disease) 489
  - Painful Heel—Bursitis (Policeman's Heel) 489
  - Ingrown Toe-nail 490
  - Halux Rigidus 490
  - Halux Valgus 490
  - Hemophilic Joint Swelling 491
- Diseases of the Joints 492
  - Dislocations 492
    - Congenital Dislocation of the Hips 492
    - Snapping Knee 495
    - Congenital Dislocation of the Knee 495
    - Congenital Hyperextension of the Knee 495
    - Congenital Dislocation of the Patella 495
    - Traumatic Dislocation of the Patella 496
    - Sacro-iliac Injury 496
    - Subluxation of the Clavicle 497
    - Congenital Dislocation of the Shoulder 497

CHAPTER PAGE

Chronic Recurrent Dislocation of the Shoulder 497
Recurrent Dislocation of the Patella 497
Dislocation of the Elbow 498
Tuberculosis of the Joints 498
Tuberculosis of the Hip 498
Tuberculosis of the Knee and Ankle 502
Synovial Tuberculosis 503
Rice Bodies 503
Tuberculosis of the Shoulder 503
Tuberculosis of the Elbow, Wrist and Ankle 503
Arthritis of the Joints 505
Arthritis—Osteo-arthritis—Arthritis Deformans . . . 505
Degenerative or Atrophic Arthritis 506
Proliferative or Hypertrophic Osteo-Arthritis . . . 507
Infectious Arthritis (Non-tuberculosis) 507
Acute Arthritis in Infancy 508
Gonorrheal Arthritis 508
Joint Deformities 510
Deformities of the Hip 510
Hip Flexion 510
Lordosis 511
Coxa Vara 511
Coxa Valga 512
Deformity of the Knee 513
Knee-flexion 513
Deformities of the Ankle and Feet 514
Postural Conditions of the Feet 514
Equino Varus (Club-foot)—Varus 514
Pes Cavus 514
Equinus 515
Equinovalgus—Valgus 516
Flat-foot—Valgus 516
Calcaneous—Calcaneovarus—Calcaneovalgus 517
Flail-ankle 517
Deformities of the Wrist and Hand 518
Madelung's Deformity of the Wrist 518
Dupuytren's Contraction 518
Congenital Club-hand 518
Other Pathological Conditions of the Joints 519
Limited Motion and Deformity of the Arms 519
Ankylosis 520
Semilunar Cartilage Displacement 521
Prepatellar Bursitis (Housemaid's Knee) 521
Loose Bodies in the Knee Joint (Joint-mice) 521
Tenosynovitis 521
Acute Synovitis 522
Intermittent Synovitis with Effusion 522
Charcot's Disease 522
Gout 522
Scapula Crepitus 523
Sprained Ankle 524
Subdeltoid Bursitis 525
Ischemic Paralysis—Contraction 525

CHAPTER PAGE

SECTION VII: DISEASES OF THE MUSCLES

I. INFLAMMATORY DISEASE OF THE SKELETAL MUSCLE . . . 527

By C. F. Hoover

Etiology 527
Symptomatology 528
  Examination of a Muscle 528
Differential Diagnosis 528
Muscular Rheumatism 530
  Symptomatology 530
Dermatomyositis 536
  Etiology 536
  Symptomatology 536
  Treatment 541
  Pathology 542
Gout 543
Myositis Fibrosa 543
Syphilitic Myositis 544
Trichinosis 545
Gonorrheal Myositis 545
Muscular Atrophy and Joint Diseases 545

SECTION VIII: DISEASES OF THE KIDNEY

I. DISEASES OF THE KIDNEY 549

By J. B. McElroy

Congenital Nephropathies 550
  Ectopic Kidney 550
  Congenital Malformations 551
  Congenital Single Kidney 551
  Congenital Atrophic Kidney 553
  Lobulated Fetal Kidney 554
  Fused Kidneys 554
  Horseshoe Kidney 554
  Fused Single Kidney 556
  Variations in Renal Pelvis and Ureters 557
Movable Kidney 558
Uremia 566
Nephropathies of Circulatory Origin 575
  Chronic Passive Congestion of Kidneys 575
Focal Atherosclerotic Kidney 584
"Bright's Disease" 585
  Nephrosis 588
  Clinical Varieties 594
Amyloid Kidney 599
Necrotizing Nephrosis 601
Glomerulonephritides 604
  Diffuse Glomerulonephritis 608
  Acute Diffuse Glomerulonephritis 609
  Chronic Diffuse Glomerulonephritis 627
  End Stage of Chronic Glomerulonephritis 637
Focal Nephritides 654
  Acute Focal Glomerulonephritis 654

CHAPTER PAGE
Chronic Focal Glomerulonephritis 656
Septic Interstitial Nephritis 656
Embolic Focal Nephritis 656
The Scleroses 657
Benign Hypertension 658
Malignant Hypertension 676
Bibliography 686

II. DISEASES OF THE KIDNEY 691

By Anton G. Rytina

Pyelitis 691
Pyonephrosis 700
Perinephritic Abscess 704
Hydronephrosis 707
Kidney and Ureteral Stone 712
Calculous Anuria 720
Cysts of the Kidney 722
Multiple Small Cysts 722
Large Serous Cysts 722
Polycystic Degeneration 723
Dermoid Cysts 725
Paranephritic Cysts 725
Echinococcus Cysts 725
Tubercular Cysts 727
Renal Tumors 727
Benign Renal Tumors 727
Malignant Renal Tumors 729
Bibliography 735

SECTION IX: DIESEASES OF THE BLOOD

I. INTRODUCTION AND CLINICAL METHODS OF BLOOD EXAMINATION

By Charles Lyman Greene

Definition 740
Functions of the Blood 740
Importance in Diagnosis 740
Morphologic vs. Chemical and Physical Examinations . . . 741
Erythrocytes 742
Abnormal Forms 743
Evidences of Regeneration 743
Unusual Erythrocytic Staining Reactions 743
The Normoblast 744
The Megaloblast 744
The Microblast 744
Mesoblasts 744
Basophilic Erythrocytes 744
Maurer's Spots 744
Schüffner's Stippling (Schüffner's Spots) 745
Howell's Bodies 745
The Leukocytes 745
Normal Leukocytic Forms 745

CHAPTER PAGE
The Polymorphonuclear Neutrophil 745
The Small Lymphocyte 745
The Large Mononuclear Leukocyte 745
The Transitional Leukocyte 745
Eosinophils 745
Basophils 745
Unusual and Abnormal Forms 746
The Metamyelocyte 746
The Myeloblast 746
Promyelocytes 746
Türck's Irritation Forms 746
Giant Marrow Cells 747
Lymphoblasts 747
Giant Lymphocytes (Pathologic Lymphoblasts) 747
Melanemia 747
Idiophilia 747
Perinuclear Basophilia 747
The Inclusion Bodies of Döhle 747
Plasma-cells 748
Essential Laboratory Procedures 748
The Coloring Matter of Blood 748
Technic of Blood Examination 748
To Obtain Blood for Examination 748
Precautions 749
Care and Preparation of Slides and Cover-glasses 749
Making the Blood Smear 749
Fixation of Dried Preparation 750
Examination of Fresh Blood 750
Examination of the Stained Specimen 751
Staining Solutions 751
Wright's Modification of Louis Jenner's Stain 751
Technic of Staining 751
Ehrlich's Triacid Stain 752
Hemoglobin 752
Tests for Hemoglobin 752
Tallqvist's Hemiglobinometer 752
Dare's Hemoglobinometer 752
Von Fleischel's Hemoglobinometer 753
Hemoglobin Estimation by Specific Gravity 753
Oliver's Hemoglobinometer 753
Gower's Hemoglobinometer 753
Sahli's Hemoglobinometer 753
The Universal Microcolorimeter 754
Directions for Estimation of Hemoglobin 756
Care and Use of Pipettes 756
Palmer's Method of Hemoglobin Determination 757
Blood-cell Count 759
The Red Count 759
The Leukocyte Count 761
Many Types of Blood Counters 762
The Thoma-Metz Hemocytometer 764
Oliver's Hemocytometer 765
The Hematocrit 766
Leukocytosis and Lymphocytosis 766
Differentiation of Leukocytosis from Leukemia 766
Average Normal Leukocyte Count 766

CHAPTER PAGE
Physiologic Leukocytosis 767
Preagonal Leukocytosis 767
Leukocytosis of Pregnancy 767
Leukocyte Count in New Born 767
Leukocytosis of Disease 767
Definition of Leukopenia 768
Lymphocytosis 768
Eosinophilia 769
Blood-platelets 769
Counting the Blood-plates 769
Determination of Hemolytic Resistance 770
Total Blood Volume 770
Coagulation Time 771

LIST OF ILLUSTRATIONS

VOLUME VI

SECTION IV: DISEASES OF THE CIRCULATORY SYSTEM.

CHAPTER IV

Disease of the Pericardium

FIGURE PAGE

1. Radiogram of Pericarditis with Effusion due to Rheumatic Infection 213
2. Radiogram of Purulent Pericarditis, secondary to Suppurative Tubercular Cervical Adenitis . . . . , . . 214
3. Radiograms of Pericardial Effusion in an Infant 215
4. Diagram giving the more frequent sites of election in Pericardial Puncture, Aspiration and Drainage 220
5. Acute Fibrinous Pericarditis 230
6. Acute Serofibrinous Pericarditis 232
7. Anterior View of Lymphosarcoma with large Mediastinal Neoplasm, also showing growth into Pericardium, Right Auricle and Right Jugular Vein (Courtesy W. B. Saunders & Co.) 240

CHAPTER VI

Instruments of Precision in Cardiovascular Studies

A. Mackenzie Ink Polygraph (From Lawson, The Heart Rhythms, Courtesy Williams & Wilkins Company) 296

B. Jaquet Polygraph (From Lawson, The Heart Rhythms, Courtesy Williams & Wilkins Company) 296

C. The Zimmerman Polygraph (From Lawson, The Heart Rythms, Courtesy Williams & Wilkins Company) 297

D. Complete Electrocardiograph, showing the manner in which the Electrodes are attached to the Patient. (From Lawson, The Heart Rythms, Courtesy Williams & Wilkins Company) . . 298

F. Auricular Fibrillation with Ventricular Extrasystoles 299

F. Auricular Fibrillation with Ventricular Extrasystoles 299

G. Slight Pulsus Alternans in Acute Rheumatism 300

H. Pulsus Bigeminus 300

I. Heart Block 301

J. Tricuspid Regurgitation 301

K. Micrograph and Polygraph 302

L. Auricular Fibrillation 310

M. Auricular Fibrillation 311

N. Aneurysmal Thrill 312

Plates i to xxiii (Figs. I–XL) showing Electrocardiographic Tracings.

SECTION V: DISEASES DUE TO PHYSICAL AGENTS

CHAPTER II

MORBID CONDITIONS DUE TO CHANGES IN BAROMETRIC PRESSURE

CHART
1. (According to Haldane.) Assuming a part becomes ½ saturated in 23 minutes, it will be 75 per cent. saturated in 46 minutes, 87½ per cent. saturated in 69 minutes, 93.75 per cent. saturated in 92 minutes, etc. 415
2. (According to Haldane.) Showing the lag in desaturation of quickly and slowly saturating parts of the body with uniform decompression 416
3. Normal oxygen dissociation curve of hemoglobin in blood. The thick line shows the extent of variation of normal curves in individuals. (After Barcroft) 432

SECTION VI: DISEASES OF THE BONES AND JOINTS

CHAPTER I

DISEASES OF THE BONES AND JOINTS

FIGURE PAGE
1. Congenital Absence of the Fibula and Deformity of the Foot . . . 452
2. Congenital Absence of Metatarsals and Toes 453
3. Supernumerary Rib 454
4. Faulty Attitude in Standing—Round Back 456
5. Round Shoulders 457
6. Scoliosis, Showing a Double Curve 458
7. Scoliosis, Showing Total Curve 459
8. Scoliosis with Rotation 460
9. Scoliosis, Showing Rotation When Patient Leans Forward . . . 461
10. Scoliosis, Right Dorsal Left Lumbar Curves 462
11. Humped Foot and Claw-foot 463
12. Supernumerary Foot 464
13. Congenital Deformity of Fingers and Webbed Fingers 464
14. Webbed Toes 465
15. Congenital Elevation of the Scapula 466
16. Rachitic Deformity. Anterior Bowing of the Tibiæ 467
17. Bow-legs Due to Rachitis 468
18. Rachitic Deformities. *X*-ray 469
19. Knock-knee Due to Rachitis 470
20. Achondroplasia 471
21. Achondroplasia, Showing Flattening of the Vertebræ 472
22. Achondroplasia. *X*-ray of the Knee 473
23. Tuberculosis of the Spine. Note the Destruction of the Bodies of the Vertebræ 474
24. Tuberculosis of the Spine with Small Kyphos 475
25. Tuberculosis of the Spine. Neglected Case, Large Kyphos . . . 475
26. Tuberculosis of the Spine. Note the Marked Kyphosis 476
27. Osteomyelitis of the Femur 477
28. Poliomyelitis. Paralysis of the Deltoid 478
29. Deformity of the Spine Due to Poliomyelitis. Note the Extreme Paralysis of the Back and Leg Muscles 479
30. Infantile Paralysis with Equinovarus Deformity 480
31. Bradford Frame and Long Calipers Applied to the Leg . . . 481
32. Spastic Equinus 483
33. Torticollis, Showing Postoperative Brace 486
34. Osteomalacia, Showing Spontaneous Fracture of the Femur . . . 488
35. Paget's Disease 489

36. Tissue and Part of Nail Removed for Ingrown Toe-Nail . . . 490
37. Hallux Valgus 491
38. Congenital Dislocation of the Hips 492
39. Congenital Dislocation of the Hip, Showing Postoperative Plaster and Position in Bed on a Bradford Frame 493
40. Congenital Hyperextension of the Knee, and Congenital Contracture of the Hip 496
41. Ankylosis Due to Tuberculosis of the Hip 498
42. Tuberculosis of the Hip 499
43. Tuberculosis of the Hip. Acute Condition 500
44. Tuberculosis of the Knee. Acute Condition 501
45. Ankylosis Caused by Tuberculosis of the Knee 502
46. Arthritis Deformans 504
47. Arthritis Deformans, Showing Involvement of the Knee . . . 505
48. Hip Flexion Deformity. Poliomyelitis 509
49. Coxa Vara 510
50. Coxa Valga 511
51. Subluxation of the Knee 512
52. Congenital Club-foot. (Equinovarus) 513
53. Club-foot. Postoperative position 515
54. Paralytic Feet (Pes Cavus) 516
55. Poliomyelitis, with Equino Valgus Deformity. Note the Shortened Extension of the Toes 517
56. Club-hand with Absence of the Radius 519
57. Ankylosis of the Hip 520
58. Gout. The thinning of the Proximal Phalanges is Shown Near Their Distal Ends 523
59. Ischemic Paralysis 524

SECTION VII: DISEASES OF THE MUSCLES

CHAPTER I

Inflammatory Disease of the Skeletal Muscles

1. Muscular Rheumatism. In this picture the patient was asked to hold his fingers and thumbs in an extended position. The photograph shows how the metacarpals of the thumbs are extended; the first and second phalanges remain in a partially flexed position. Both ring fingers are also in a partially flexed position at the metacarpal phalangeal joint 532
2. Muscular Rheumatism. This picture shows the diminution in volume of the leg muscles and the smooth, indurated and bronzed skin; the same characteristics of the skin and muscles of the forearm are apparent 533
3. Muscular Rheumatism. The picture shows the prominence of the sternocleidomastoid muscle on the left side. This prominence is due to shortening of the muscle from fibrous degeneration in its lower third 534
4. The patient standing erect and was told to activate both quadriceps muscles. The eminences at the middle of both thighs mark the locations of the proximal end of the ruptured quadriceps muscles 535
5. The patient is trying to flex the head on the the trunk, to throw the arms in the horizontal position, to bend the trunk on the thighs, and also to bend his knees 539
6. The patient is trying to bend the head backward, to throw the arms upward, and to bend the trunk backward on the hips . . . 540

SECTION IX: DISEASES OF THE BLOOD

CHAPTER I

INTRODUCTION AND CLINICAL METHODS OF BLOOD EXAMINATION

FIGURE PAGE
1. Davis Hemoglobinometer 753
2. Von Fleischel's Hemoglobinometer (Miescher's Modification) . . . 754
3. Oliver's Hemoglobinometer 755
4. Sahle's Hemoglobinometer 755
5. Kuttner's Pocket-size Colorimeter 756
6. Ruling of the Gorgajen-Papenheim Counting Chamber 759
7. Thoma-Zeiss Blood Counter, showing Pipette, Counting Chamber and a part of the ruled field 759
8. Thoma-Zeiss Ruling 760
9. Neubauer's Ruling 760
10. Vertical Longitudinal Section of Slide, with cover glass in position, showing new method of construction 762
11. Thoma-Levy Counting Chamber with original Thoma ruling . . . 763
12. Thoma-Levy Counting Chamber, Bürker type with two Neubauer rulings 763
13. Mixing pipette for red corpuscles 764
14. Mixing pipette for white corpuscles 764
15. Hemacytometer (the Thoma-Metz) 764

PRACTICE OF MEDICINE

VOLUME VI

SECTION IV

DISEASES OF THE CIRCULATORY SYSTEM

CHAPTER I

DISEASES OF THE ARTERIES AND CLINICAL BLOOD-PRESSURE

By Louis M. Warfield, M.D.

Arteriosclerosis, p. 2:—General definition and etiology, p. 2; General anatomy of the arteries, p. 2; Physiology of the arteries, p. 4; Etiology, p. 5; Symptomatology, p. 7; Diagnosis, p. 10; Complications, p. 11; Association with other diseases, p. 11; Treatment, p. 12; Prognosis, p. 12; Pathology, p. 13.
Thrombo-angiitis obliterans, p. 15:—Definition, p. 15; Etiology, p. 15; Symptomatology, p. 16; Diagnosis, p. 17; Complications and sequelæ, p. 17; Treatment, p. 17; Prognosis, p. 17; Pathology, p. 17.
Syphilitic Arteriosclerosis (Arteritis), p. 18.
Syphilitic aortitis, p. 19:—Definition, p. 19; Etiology, p. 19; Symptomatology, p. 19; Diagnosis, p. 21; Treatment, p. 21; Pathology, p. 22.
Aneurysm, p. 23:—Definition, p. 23; Etiology, p. 24; Symptomatology, p. 26; Diagnosis, p. 32; Clinical varieties, p. 32; Treatment, p. 34; Prognosis, p. 35; Pathology, p. 36; Historical summary, p. 36.
Thrombosis of the coronary arteries, p. 36:—Definition, p. 36; Etiology, p. 36; Symptomatology, p. 37; Diagnosis, p. 37; Complications, p. 38; Clinical varieties, p. 38; Treatment, p. 38; Prognosis, p. 38; Pathology, p. 39.
Periarteritis nodosa, p. 40:—Definition, p. 40; Etiology, p. 40; Symptomatology, p. 40; Diagnosis, p. 40.
Clinical blood-pressure, p. 41:—Definition, p. 41; Technic of blood-pressure measurements, p. 42; Mechanism and maintenance of blood-pressure, p. 43; Average normal blood-pressure, p. 46; Functional tests in relation to blood-pressure, p. 49; Hypotension, p. 52; Hypertension, p. 53; Occurrence in various conditions, p. 62; Value of blood-pressure estimations, p. 65; Bibliography, p. 65.

ARTERIOSCLEROSIS

General Definition and Etiology.—Arteriosclerosis cannot strictly be called a disease *sui generis*. It is rather a degeneration of the arteries due to a variety of causes, most of them not yet altogether established. The various causes result in degeneration of the coats of the arteries with the production of fibrosis, or calcification, or both, with changes in the length and caliber of the vessels. Chief among the causes are *syphilis*, the *infections*, and some *infectious diseases*. *Heredity* probably plays a large part in determining the quality of the arterial tissue with which the individual begins life. In other words, arteriosclerosis is a chronic degenerative result of disease in which the arteries of the body are affected. Not only the arteries, but also the capillaries are affected, as Gull and Sutton long ago showed; this observation led them to assign the name "arteriocapillary fibrosis" to the degenerative changes.

ARTERITIS.—Acute inflammation of the arteries has never been observed except as an extension of inflammation occurring in neighboring parts. In this respect the arteries differ from the veins. The nearest approach to acute arteritis is the usual disease known as periarteritis nodosa.

CHRONIC INFLAMMATIONS AND DEGENERATIONS.—These are common. Lesions are found varying in size and degree from small isolated patches in the intima of the aorta to extensive calcification of the coats of the large vessels and obliteration of the smaller ones. It will be convenient to describe the chronic lesions under the following headings:

1. Arteriosclerosis
2. Thrombo-angiitis obliterans
3. Syphilitic arteritis (arteriosclerosis)

General Anatomy of the Arteries.—In order to gain a clear conception of the lesions in the arteries, it is essential to bear in mind the anatomical peculiarities of the arteries, from the aorta to the capillary. The structure of the artery has much to do with determining the character and extent of the pathological process in which it may become involved.

The aorta and the largest branches are merely highly elastic distributing tubes. Three coats are described: (*a*) the adventitia, (*b*) the media, and (*c*) the intima, respectively, outer, middle and inner coats. The intima consists typically of endothelium reinforced by a variable amount of elastic tissue in which the elastic fibers predominate. The tunica media is composed of intermingled bundles of elastic tissue, smooth-muscle fibers, and some fibrous tissue. The adventitia is exceedingly tough. It is usually thinner than the media, and is composed of fibro-elastic tissue. This division, while necessary for descriptive purposes, is somewhat arbitrary, as it is difficult to discover any distinct separation into layers, particularly in the larger arteries.

The muscular layer varies from single scattered cells in the arterioles to bands of fibers making up the body of the vessel in the medium-sized arteries.

There is elastic tissue in all except the smallest arteries. It varies in amount from a loose network to dense membranes. In the intima of the larger arteries the elastic tissue is formed in sheets, which, under the microscope, appear to be perforated and pitted—the so-called fenestrated membrane of Henle.

All the arteries except those one millimeter in diameter or less are supplied with intrinsic blood-vessels, the vasa vasorum which enter the adventitia. The outer coat and the outer portion of the media are supplied with blood by these vessels. The intima and the inner portion of the media obtain their nourishment from the blood flowing in the artery. Lymphatics and nerves are also present in the outer and middle coats of the arteries. From the aorta to the capillaries the arterial structure undergoes profound changes which, in any particular set of vessels, although gradual, are yet definite.

The aorta is composed almost entirely of layers of elastic tissue. The intima lies on a dense membrane; the media is composed of layers of elastic tissue arranged both longitudinally and circularly, and the adventitia consists in particularly tough fibre-elastic tissue. The coefficient of elasticity of the normal aorta is physically perfect. Functionally it is the large blood-distributing tube, which, by its elastic recoil, keeps the blood in motion during the diastole of the heart. Gradually more muscle and less elastic tissue are found, so that in the radial, for example, the endothelium is seen under the microscope as a delicate line, on which a few nuclei are visible. The media is comparatively thick, and is composed of muscle-cells, arranged in flat bundles, and plates of elastic tissue. Between the media and the externa, the elastic tissue is somewhat condensed and forms the external elastic membrane. "Followed toward the capillaries, the coats of the artery gradually diminish in thickness, the endothelium resting directly upon the intimal, elastic membrane, as long as the latter persists, and afterward upon the rapidly attenuating media. The elastica becomes progressively reduced until it entirely disappears from the middle coat, which then becomes a purely muscular tunic, and, before the capillary is reached, is reduced to a single layer of muscle-cells. In the precapillary arterioles the muscle no longer forms a continuous layer, but is represented by groups of fiber-cells that partially wrap around the vessel, and are at last replaced by isolated elements. After the disappearance of the muscle-cells the blood-vessel has become a true capillary. The adventitia shares in the general reduction, and gradually diminishes in thickness until, in the smallest arteries, it consists of only a few fibro-elastic strands outside the muscle-cells" (Piersol's *Anatomy*). The capillaries, composed only of endothelium, have always been considered passive tubes without power of contraction or expansion. Koegh has recently presented evidence which casts doubt upon the purely passive part played by capillaries in the nutrition of organs and tissues. The structure of these minute vessels consists in a single layer of cells, the cell substance being arranged in strands running from the nuclei around the capillary. Contraction of a cell may occlude the capillary. Koegh also showed that the maximum amount of blood which can be present in a capillary area is at least 750 times the minimum. Furthermore, he demonstrated that blanching of the skin, blushing, and blanching and hyperemia of organs, are dependent upon the contraction or dilatation of capillaries. It has also been suggested (Dale and Richards) that there is a mechanism capable of regulating capillary tone. The lumen of a capillary is only the diameter of a red blood-corpuscle, 7.5 micra, and very slight contraction on the part of the encircling cell may be sufficient to obliterate the lumen. The blood-color of any tissue is actually dependent upon the filling or emptying of the capillaries, rather than upon the state of the arterioles.

Physiology of the Arteries.—The fact that the large arteries are composed mainly of elastic tissue renders them ideal as distributing channels. This is the only function which they possess. Their perfect elasticity enables them to gradually absorb the systolic force of the heart-beat, and the elastic rebound of the aorta, during diastole of the heart, keeps the blood flowing evenly. In the terminal branches of the arterioles, where the muscle-tissue predominates, there is opportunity for great expansion and for strong contraction. The vasomotor fibers of the sympathetic system which leave the cord in the dorsal region, control the contraction and expansion. The large splanchnic area is capable of holding an enormous amount of blood, as are also the skin-vessels in the dermis. The blood actually comes in contact with the tissue-cells, and the interchange of gases and nutrient and excrementitious substances occurs in the extensive capillary area. The veins simply collect the blood and return it to the right side of the heart.

The pulmonary circulation probably acts in much the same way as the systemic circulation. No vasomotor fibers have ever been conclusively demonstrated in the pulmonary arterial branches, but there is abundant reason to believe that they are present and will eventually be demonstrated. However, the anatomical structure of the pulmonary capillaries is essentially the same as that of those found elsewhere in the body, and there is no reason to believe that they too are incapable of responding by contraction or dilatation to influences acting upon them. That they do become greatly dilated is a common postmortem observation.

As the individual advances in years, there are normal changes in the arteries which lead to thickening and inelasticity of the walls. In any estimation of the state of the arteries, especially by microscopical examination, this fact should be kept in mind. Thayer and Fabyan found that the changes in arteries are definite from birth to old age. In general, the artery becomes strengthened by the development of new elastic fibers in the intima, and of connective-tissue in the media and adventitia. During the third and fourth decades of life, there is also a distinct thickening of the connective-tissue in the intima. By the fifth decade the deposits of connective-tissue in the intima are marked, and there is an increase of fibrous tissue upon the medial side of the intima, and, in lesser degree, throughout the media. "Finally, in these sclerotic vessels, degenerative changes set in, which are somewhat different from those seen in the larger arteries, consisting, as they do, of local areas of coagulation-necrosis with calcification, especially marked in the deep layers of the connective tissue, thickenings of the intima, and in the muscle-fibers of the media, particularly opposite these points. These changes may progress to actual bone formation."

The mesenteric artery differs in some respects from the radial artery, but, in the main, the changes brought about by age are the same in both. There are two striking points of difference: "(1) Calcification (in the mesenteric artery) is apparently much less frequent than in the radials; (2) in several cases plaques were seen with fatty softening of the deeper layers of the intima and superficial proliferation—a picture never seen in the radial."

It has also been found that, in general, after the age of thirty-five the muscle of the media begins to exhibit fatty degeneration. After the age of fifty this condition is well marked. Furthermore, fatty degeneration may yield at this time to a calcareous infiltration, or the fibers may undergo complete absorption. Consequently, it appears that the thinning of the aortic media is not due so much to the atrophy of the elastic tissue as to that of the muscle tissue. The former, however, loses its specific property, and the artery thus becomes practically a connective tissue tube. In very many cases it is practically impossible to draw the line between the changes which are physiological, i.e., due to the aging of the tissues, and those which are pathological.

The limitation of the blood supply to the various organs, including, of course, the heart, is the natural result of the changes which take place in the arteries as age advances. Tubes which are more or less unyielding, or which are fairly rigid, cannot serve as competent distributing channels for an intermittent force-pump system. General atrophy of all organs necessarily must and does occur, and a decreased activity of the individual results. This is "old age." Some individuals who have excellent arterial tissue as an inheritance, and who have not abused the tissues, may postpone such changes as have been described for a longer period than the average. On the contrary, those who begin life with poor arterial tissue—"vital rubber," Osler has called it—and who further abuse the tissues, may be old long before the average.

Etiology.—Causative Factors.—When one begins to describe the causes of arteriosclerosis, one finds many theories but few actually proven facts. Men and women of advanced age are frequently seen who have relatively soft arteries. On the other hand, definite pathological changes in the arteries are found in infants. There can be no doubt that heredity plays a prominent rôle in the determination of arterial changes in the individual. The reasons for this are wholly unknown, but the fact remains that all do not begin life with equally resistant arterial tissue. One may thus divide the types of causes broadly into (1) congenital, and (2) acquired.

Congenital.—Possibly this type should not be separated from the general form. However, when evidences of advanced sclerosis and small aneurysms are found in infants, it is difficult to ignore the congenital origin of the sclerosis. Children born of syphilitic parents show certain stigmata, among which are sclerosed arteries. Therefore, it appears to be correct to speak of a congenital form of arteriosclerosis, meaning the type in which there is transmission to the offspring of inferior tissue. Changes appear so early in life that there is a gap of some years between the development of this form of sclerosis and of that caused by conditions affecting the person after birth.

Acquired.—No one cause produces arteriosclerosis. The fatty atheromatous plaques on the aorta and on the large vessels which include only the intima are caused by various febrile diseases. They have no particular significance. Infectious diseases, especially those of prolonged cause and complicated with pyogenic cocci, have been regarded as factors in the production of arteriosclerosis. A study of 500 inmates of a County Poor House, with particular reference to infectious disease and palpable arteries, demonstrated this to be a negligible factor. For example, there were 252 individuals between the ages of thirty-eight and eighty years who had no palpable sclerosis; 248 with sclerosis; 147 who had serious infections, but who had no sclerosis; and 180 who had infections with sclerosis.

It is generally believed that certain products of incomplete intestinal digestion of proteins are absorbed into the blood and there produce widespread contraction of small arterioles and capillaries. This naturally requires greater effort on the part of the heart, the force of its beat is greater, the blood-vessels are more violently stretched and strained and, according to Adami's terminology, "strain hypertrophy" of the vessel-walls results. The vessels may here and there show lesions which are replaced by nodules of fibrous tissue. Or the whole vessel may be so strained as to produce a diffuse fibrous thickening of the media and subintimal layers. The vessel either stretches and becomes tortuous, or it contracts and becomes firm to the touch. In either case, it is the subject of diffuse fibrous change.

To this form of arteriosclerosis caused by increased peripheral resistance Allbutt has given the name hyperpietic (increased "squeezing"). He considers that the hypertension (hyperpiesis) is the cause of the arteriosclerosis. This conclusion is correct, perhaps, in some cases, but not in all.

The senile form, that of pipe-stem, beaded arteries, is a concomitant of *advanced age.* It affects both males and females, the anchorite and the libertine. No race is exempt. It is not always present in those of advanced years, but it is seldom found except in the aged. Men in the fifties are seen with beaded arteries, but this is not common. In fact, the etiology of this form of arteriosclerosis is quite unknown. It is not the late result of hypertension. The blood-pressure is normal or low. The heart is small and the muscle shows the degeneration known as brown atrophy. All the organs are atrophic and function poorly. This is expressed in the individual by thinness and slow movement. Other factors which have been blamed for arterial degeneration are alcohol, lead and tobacco. As far as alcohol and tobacco are concerned, it must be admitted that there is no proof of their relationship to arteriosclerosis. There are impressions and ideas by the dozen, but there is no demonstrable proof.

There seems to be some evidence that *lead* is a causative factor.

Although no one has ever been able to produce any lesions in the arteries of animals with lead salts, yet there is abundant and very excellent evidence that arteriosclerosis is caused by prolonged 'contact with lead. Again, one must not be misled into believing that every worker in lead will have arteriosclerosis. This is far from the truth. That indefinable something which we call heredity plays some part. Soap and water, toothbrushes, and regular visits to dentists are factors in preventing the development of the disease.

Certain chronic metabolic disorders, such as *gout* and *diabetes,* are said to favor the development of degenerative changes in the arteries.

Muscular work day after day and year after year, may produce arteriosclerosis of the nodular (the aorta) or of the diffuse form, or very frequently a combination of the two.

Great *mental strain* coupled with *overeating*—factors found in the lives of many of us—apparently cause early arterial degeneration. Coffee and tea are not concerned in the production of arteriosclerosis.

Where involuntary processes in the arteries are associated with advancing years, arteriosclerosis may be most extensive, and yet there may be no symptoms, inasmuch as these are dependent entirely upon the organ or organs which are affected by the change in blood supply due to the vascular sclerosis. It is doubtful whether the changes in the arteries are ever uniform throughout the whole vascular tree. Wherever they are greatest the symptoms will be most prominent.

Symptomatology.—General Symptoms.—There is a sense of early fatigue both in body and in mind. There is often an unusual intolerance of alcohol or tobacco. Vertigo is frequent; there is ringing and roaring in the ears. There may be a dull headache; irritability and somnolency, or the opposite, insomnia, are found in some cases; headache is often increased by mental effort. Numbness and tingling of the hands, arms, feet, or legs and neuralgias, which follow the arteries, are not infrequent. All such symptoms are found in other conditions, for instance in neurasthenia.

Mild dyspeptic symptoms are also found, such as heartburn, belching, and a feeling of weight in the epigastrium. There is subacidity and sluggish gastric mobility. Attention has been called to an unnatural pallor of the face in early arteriosclerosis. Progressive emaciation, unaccompanied by any gross pathological lesion, is also found. It is essential to keep constantly in mind the conception that arteriosclerosis is not a disease in the strict sense of the term and that its symptoms are only indications of disturbed blood supply. Perhaps the most evident and distinct symptoms are those noted in the nervous and cerebral organizations. In the former (not always to be differentiated from neurasthenia) the prodromal symptoms may be expressed in the patient by a tendency to introspection, by a feeling of regret for things done or undone, and by a curious uncertainty as to the future. Changes in mental attitude are often most noticeable to the family. An amiable man becomes irritable, a timid man bold in affairs, an even-tempered man flies into fits of anger, a tolerant man becomes jealous. Trifles are magnified until they appear to occupy the patient's whole thought. There is uncertainty of conclusion, lack of reasoning power and hesitancy in action. In cerebral arteriosclerosis a gradually progressive mental deterioration, associated with so-called "patchy memory" is the most characteristic symptom. A gradual failure of mental processes is noted. Insight into the mental condition is lacking, the judgment is poor, and restlessness, mental confusion and delusions of persecution possess the patient.

HYPERTENSION.—The symptoms associated with increased blood-pressure in arteriosclerosis are no more distinctive than those usually found with normal pressure and beaded arteries. How often are we asked by patients, with health evident in every gesture, to examine them, because recently they were told by life insurance examiners that their blood-pressure was high? Such subjects are not only free from symptoms, but they stoutly affirm that they are absolutely well. Great degrees of compensated hypertension are found in patients who have no symptoms. In fact, except for the associated changes on the part of the brain, heart, and kidney, from which organs the most important symptoms arise, there are few actual symptoms due to hypertension *per se.* Among these the most constant are headache with pounding in the ears, especially noticeable in bed at night, and, occasionally, some flatulence. But dyspnea on exertion, edema, nycturia, etc., belong to cardiac and renal breakdowns.

Frequently the patient complains of failing eyesight, and the ophthalmologist, in the course of the examination of the fundus of the eye, makes the diagnosis. Bardsley considers that there are essential differences between the appearance of the fundus in simple transient high tension and in the high tension of arteriosclerosis. He makes the following distinctions:

In simple high tension:

(1) The blood-vessels have an appearance of uniform distention and fullness.

(2) The light streak is broadened out; it may be greatly increased, apparently reaching almost the whole breadth of the vessel.

(3) The light streak is very much brighter than normal, the bril-

liancy increasing with the rise of the tension, until with very high tension it becomes like bright copper wire (not silver wire).

(4) The tight arteries indent the veins; with medium high tension, they indent them slightly, with very high tension they indent them deeply, leading to back-pressure and all its consequences.

In arteriosclerotic high tension:

(1) There is *irregular* tortuosity, especially of the smaller twigs.

(2) There is increased brilliancy of the light streak, while at the same time the latter appears *narrower* and more central.

(3) Irregularity of caliber and beading are sure indications of sclerosis.

(4) General diminution in size of vessels and "silver wire" reflex show advanced sclerosis.

ANGINA ABDOMINALIS.—In elderly people, who are subjects of arteriosclerosis, there is a train of symptoms—which are, however, not common—indicating a condition to which Baccilli gave the name, *angina abdominalis.* The attack occurs in the case of patients who have aneurysmal dilatations of the branches of the celiac axis or who have arteriosclerosis of these vessels, namely, the gastric, splenic, and superior mesenteric arteries. The onset occurs suddenly and violently in the midst of good health. The pain, like that of angina pectoris, is agonizing, of short duration, is located in the midline around the umbilicus, is accompanied by flatulence, great anxiety, restlessness, and is followed by profuse sweating. Men are more prone to the attacks than women. The exciting cause of the seizure is usually exertion (even slight) or the overloading of the stomach. The attack may occur at any time of the day or night. There is no fever, and, as a rule, no vomiting, but there is nausea.

On examination acute tenderness around the umbilicus and general abdominal soreness are found. Such a condition must be differentiated from the crisis of tabes dorsalis, from the acute inflammatory diseases of the upper abdomen and from the pain of gastric or duodenal ulcer. Differentiation is not always easy.

THROMBOSIS OF THE MESENTERIC ARTERIES.—Ingebrigsten found 2 cases of this unusual condition at autopsy, in both of which the superior mesenteric artery was thrombosed. Neither patient had shown symptoms of such a condition during life. The vessels in both cases were luetic.

The symptoms, as a rule, are as follows: Pain, vomiting, collapse, bloody stools, meteorism, rapid pulse and subnormal temperature. Thevenat and Rey report a case in a man of sixty-seven who had arteriosclerosis. The intestine supplied by the thrombosed artery formed a large abdominal tumor, which developed very suddenly. Pain and collapse with the sudden appearance of the tumor were the prominent symptoms and signs.

Diagnosis.—The diagnosis of arteriosclerosis is mainly one of exclusion. That is to say, all means should be employed to discover some other basis for the symptoms before the final diagnosis is made. Arteriosclerosis is such a comprehensive and high-sounding name that it is satisfying to both physician and patient. A man with cancer, or primary anemia, or tuberculosis of the lungs, or some neurological disease, or syphilis, etc., may have easily palpable arteries and complain of all of the symptoms which characterize simple arteriosclerosis.

In palpating the radial artery to discover the presence of thickened arteries, certain precautions should be observed. In a thin person the normal artery can often be felt against the radius, if one simply rolls the artery under the fingers of one hand. To palpate the artery both hands should be used. One finger presses the artery near the base of the thumb in order to shut off the pulse which may come through the palmar arch from the ulnar artery. The artery is then stripped proximally, the pulse is shut off by a finger of the other hand and the empty vessel is then palpated between the two points of pressure. The combination of enlargement of the heart downward and to the left with heaving impulse, a sharply accentuated second sound in the aortic area, and thick, fibrous arteries, is pathognomonic of arteriosclerosis with hypertension. The early signs of this condition are not easily discoverable. As a rule, these cases of arteriosclerotic hypertension occur for the most part in men who have been athletes and then have settled down to a life of business cares and mental strain. Overeating undoubtedly plays a large part in the development of the arterial diseases. The arteries of people prone to such indulgence are large and fibrous and are easily palpable. The enlargement of the heart, the increased systolic and normal diastolic pressure, and the easily palpable arteries, should at once direct attention to the probable diagnosis. Until people go to their physicians, for regular yearly or semi-annual examinations, these cases will not be discovered in the early stages, except the few which are disclosed in routine life insurance examinations. (See chapter on Blood-pressure.)

It has been said by some that the combination of enlargement of the heart downward and toward the left, with a ringing second aortic sound, is pathognomonic of arteriosclerosis. This is true of the arteriosclerotic hypertension group. It holds true to some extent for the essential hypertension group, except that the heart is not as far toward the left; it does not hold true for the senile arteriosclerotic form.

Arteriosclerosis will rarely be seen by the physician except in the advanced form until men and women seek the physician for yearly or semi-annual examination as stated above. Then the initial palpable arteries, the slight hypertrophy of the heart, and the early accented second aortic sound, together with the increased blood-pressure, will direct attention to the insidious malady.

The early neurasthenia and the early mental symptoms of senile arteriosclerosis will have to be differentiated from true neurasthenia (nerve exhaustion), psychasthenia, pulmonary tuberculosis, cancer, etc.

Frequently the only symptom noted is failing vision, and the alert ophthalmologist makes the diagnosis from the examination of the ocular fundi.

Complications.—The complications of arteriosclerosis consist in the accidents which occur to stretched or ruptured arteries, gradual thrombosis with loss of function of the part, and myocardial changes.

Collins and Zabriskie reported a case of arteriosclerosis of the spinal cord with symptoms referable to the loss of the blood-supply to the lumbar enlargement of the cord.

Occasionally the condition known as "intermittent claudication" is observed. Sufferers from this complication can walk slowly with little or no difficulty. However, if the patient hastens there is pain in one or both legs and, finally, inability to walk. After a variable period of rest the victim again recovers the use of his legs. The presumption is that the condition is due to the thickness and narrowness of the arteries, through which only enough blood passes to supply the muscles when at rest or on very slight exertion. With any extra exertion, there is a call for more blood, which cannot reach the muscles; then there is a spasm of the arteries and relative anemia of the muscles. A period of rest, therefore, restores the circulation and the use of the muscles.

Gangrene, usually of the dry, mummifying type, is not infrequently seen in the fingers or toes, or even on the whole foot. In such cases there is *endarteritis obliterans,* or there may be *thrombo-angiitis obliterans.* Other complications which affect the brain, the kidneys, and the heart are considered elsewhere in the sections dealing with the diseases of these organs. Raynaud's disease may be associated with arteriosclerosis.

Association with Other Diseases.—Arteriosclerosis is a chronic process, does not necessarily give rise to symptoms, and is compatible with considerable activity. Consequently, it may be found associated with any disease known to us. It modifies the prognosis in diseases such as pneumonia and prolonged fevers very materially. The author believes that a distinction should be made between arteriosclerotic hypertension, the essential hypertension (hyperpiesis of Allbutt), and arteriosclerosis of the senile type. The conditions are not the same, and they are not stages of the same process. They are separate entities.

In arteriosclerotic hypertension the arteries are large and tortuous. The pulse-wave is large and the vessels are elongated. In essential hypertension the artery is not tortuous, the wall is firm (feels like whip cord), and the pulse-wave is not very large. In senile arteriosclerosis the arteries are tortuous, beaded, almost incompressible, due to the circular plaques of calcification, and the pulse is feeble and small. When we speak of arteriosclerosis, then, what do we mean? We cannot have in mind all three of these varieties. Our terminology is loose. We should make our terms more explicit. It seems best to restrict the term arteriosclerosis to the form in which blood-pressure changes and enlargement of the heart are not present. This would confine the term to the senile form. Another form would be the arteriosclerotic hypertension. As for the essential hypertension group with arteriosclerosis, there is still a difference of opinion as to whether the sclerosis precedes the cardiac hypertrophy or is the result of the hypertrophy. Sir Clifford Allbutt holds the former view, and it seems that his conclusion has the weight of evidence in its favor. Now, since there are some experimental data which reveal a blood-pressure-raising substance in the cortex of the adrenals, and since there is evidence of contraction of capillary areas resulting from circulating poisons, this viewpoint is further substantiated. Therefore, sclerosis is the initial process, while cardiac hypertrophy follows the attempt on the part of the heart to compensate for the widespread resistance to the blood-flow, caused by thickened and more or less inelastic vessels.

Hence, there are three clinical varieties of general arteriosclerosis:

1. The arteriosclerotic hypertension.
2. The essential hypertension.
3. The senile hypertension.

If we keep these distinctions in mind, we shall at least define our terms more accurately. The syphilitic form is purposely excluded from this classification. It is a special form and will be treated separately.

Treatment.—The most efficacious treatment is prevention. We cannot cure old age and we can do little for the advanced hypertension type except by giving sound advice as to diet and mode of life. Extensive propaganda is necessary to convince people that it is just as important to inventory their bodies every year as to inventory their stocks in business. We shall never be able to fulfill our obligations to the public until we succeed in persuading them of the absolute necessity for regular physical examinations. Preventive *prophylaxis* is essential.

The treatment of arteriosclerosis is so intimately connected with the treatment of hypertension that the question will be handled fully in the section dealing directly with hypertension. Likewise, the accidents resulting from sclerosis of the cerebral vessels and the results of the various other complications are discussed in the several sections dealing with those subjects.

In the senile form of arteriosclerosis, no drugs are of any special value. Usually the pipe-stem arteries are found in a routine physical examination and have little to do with the patient's illness. **Diet** of a simple nature, **attention to the bowels** and rational **hygiene** are the only necessities in cases of this kind.

Prognosis.—In a chronic progressive condition like arteriosclerosis, which is a natural consequence of advancing years, and which may be caused in younger life by a number of agencies, the prognosis is difficult. In the senile form, the afflicted person may live for years very comfortably. When cerebral changes begin, the prognosis is rendered more grave. However, old people with cerebral arteriosclerosis may live in asylums for several years. When hypertension and arteriosclerosis are combined in the arteriosclerotic hypertension group, the prognosis depends entirely upon the ability of the heart to carry on the circulation. Only when definite signs of cardiac decompensation appear may one begin to make a prognosis. Although the author has seen patients subject to this disease live for nine years, three years is usually a long time. Very much depends upon the circumstances of the patient—upon his ability to carry out instructions, and his willingness to coöperate with the physician. Those with financial comforts have a better chance of recovery than those who are compelled to labor from day to day.

In the type characterized by small wire arteries and very high tension, the prognosis is most uncertain. At any time and under any circumstances there may be a rupture of a cerebral vessel with consequent paralysis or sudden death. It is quite impossible to predict a cerebral accident or a failure of the heart-muscle; the most that can be said is that in this type there are more cerebral apoplexies than in any other type, and, therefore, the possibility of cerebral accident is always present. Some individuals suffer from apoplexy, recover partially, and live for many years, although they retain a limp and eventually die of cardiac failure.

Pathology.—Microscopic changes are found in the aorta and large branches, varying from irregular yellowish white elevated streaks, including only the intima, to large calcified plaques, including the intima and most of the media. In all prolonged fevers intimal and subintimal changes have been found in the large vessels. They have been found most recently in 98 out of a total of 120 cases of influenzal pneumonia. The lesions "appeared as opaque, pale yellowish, or light orange yellow, narrow, firm streaks and corrugated ridges, generally occurring longitudinally on the posterior wall of the aorta." The lesion was in the deepest layer of the intima, which was fibrous and swollen. Large cells with degenerated and vacuolated cytoplasm were found, which, in places, had apparently fallen out, leaving small ragged walled areas. For the most part these have no significance. The changes which lead to the general thickening of the whole artery, such as the radial, are deeper, involve the superficial layers of the media, and result in deposition of fibrous tissue. In the nodular form the lesions are found on the aorta and large branches, particularly at or near the orifices of branching vessels. These nodules may be quite large. They are of yellowish white color. They are usually most numerous in the abdominal aorta. The initial lesion is in the media, and consists of an actual dissolution of this coat, with rupture of the elastic fibers and infiltration with small round-cells. Coincidently, there is intimal proliferation and some connective tissue growth in the adventitia. The process may cease here, leaving a nodule or a flat plaque on the vessel, or necrosis may set in, resulting in a collection of degenerated cells and fat composing the so-called atheromatous abscess. There are no pus-cells in these "abscesses." Rupture leads to shallow ulcers at the base of which calcified deposits are often found later on. As there is no inflammation, there are no new vessels and no granulation tissue to contract later and leave scars.

Another type of lesion, known as the Moenckeberg type, consists of depressions which may encircle the branches of the aorta; the depressions are due to the degeneration of the middle coat, cause bulgings here and there, and give the vessel a beaded appearance. If such an artery is held to the light, the sacculated spots are seen to be much thinner than the surrounding artery. Calcification of the thinned media often results. The arteriosclerotic process is rarely uniformly distributed. Marked fibrous sclerosis of the radials may occur without great changes in the aorta. However, the senile form, in which nodular and calcified plaques are found, is usually widespread, affecting the arteries of the brain and the coronary arteries as well.

Naturally, the arteriosclerotic process varies in arteries of different structure. Where the media is muscle, large nodular plaques are not possible. Intimal proliferation, mesial lesions leading to the thinning of the wall in spots and calcification of the media are found. Occasionally there is degeneration of the media and replacement by connective tissue with or without hypertrophy of the intima. In the arterioles the hypertrophy of the intimal tissue may lead eventually to occlusion of the vessel, the endarteritis obliterans. When the aorta is the seat of nodular and calcified sclerosis, it is dilated, somewhat tortuous, and inelastic. Such a condition is called endarteritis deformans. In endarteritis obliterans the microscope shows an accumulation of cells, usually on one side of the lumen, so that a nodule is produced which projects into the lumen of the vessel.

Occasionally the hypertrophy of the intima is seen to extend completely around the vessel, but in such a case it is always more evident at one particular spot in the lumen.

In the arteriosclerotic form, the media of the large vessels, radial, ulnar, temporal, tibials, etc., undergoes weakening here and there. The vessels become elongated, and fibrous tissue is deposited rather widely throughout the media. The adventitia is also thickened. The vessels become larger and more tortuous than normal. Experimentally, lesions have been produced in the aorta of animals, chiefly rabbits, by a variety of substances injected intravenously. Josne was the first to produce lesions in the media of the rabbit's aorta by adrenalin. This effort was soon confirmed. However, much of his work was discredited when it was shown that spontaneous lesions of a similar nature were found even in young rabbits. The essential lesion in the adrenalin sclerosis is degeneration of the muscular and elastic tissue of the media with consequent production of aneurysm. Some experimenters have been able to produce plaques in the aorta, affecting mainly the media, by traumatizing the vessel and then injecting cultures of *Bacillus typhosus.* Traumatism alone is not sufficient. There must be a *locus minoris resistentiæ,* plus the infective agent. Injections of *Staphylococcus aureus,* streptococcus, *Bacillus typhosus, Bacillus diphtheriæ,* barium chlorid, nicotin, etc., into guinea pigs and rabbits has occasionally resulted in small lesions commencing in the adventitia, and depending upon disease of the vasa vasorum. These lesions are in no sense comparable to the arteriosclerosis of man. By repeated injections of staphylococcus into the rabbit small plaques of fibrous thickening and fatty degeneration of the intima of the aorta have been produced. Occasionally there were small nodules of cellular connective tissue with calcification in the upper media. These changes are generally proliferative. With *Bacillus diphtheriæ* the lesions are degenerative. Injections of this organism, combined with injections of pituitrin in an attempt to produce increased blood-pressure, have resulted in a vascular degeneration involving the entire aorta, the carotids to the base of the skull, the subclavians and iliacs, and, for a varying distance distally, the brachials, femorals and large abdominal vessels. The first part of the pulmonary artery is sometimes affected. The lesion is practically diffuse throughout the aorta and the vessels previously mentioned, and consists of a fatty degeneration and necrosis of the smooth muscle in a wide zone of the media, as well as in a concentration of the elastic fibers in the region affected. This produces an irregular thinning of the vessel-walls and many small aneurysmal pouchings. This corresponds somewhat to the Moenckeberg type of arteriosclerosis in man, although there is a marked difference in the medial lesions, due to the much thicker media in man. Extensive calcification also occurs throughout the degenerated zones, both in the aorta and in the large vessels.

Putrefying meat and the ethereal ester of bacterial putrefaction have been fed to dogs and to guinea pigs and monkeys. Some arterial changes were found, such as inflammation and degeneration of the media and adventitia in connection with hyperplasia and calcification of the intima.

Critical analysis of all the changes thus far produced by the injection of poisons or by the feeding of various substances shows that no one has yet produced in animals lesions analogous to those produced in man, with the possible exception of the lesions noted above of the Moenckeberg type, produced by the combination of diphtheria bacilli and pituitrin.

THROMBO-ANGIITIS OBLITERANS

Definition.—This is an affection occurring for the most part among young adult Russian and Polish Jews, and is characterized by the inflammation and obliteration of both the arteries and the veins of the legs and by a subsequent canalization in cordlike remnants of the blood-vessels.

Etiology.—The actual cause of the disease is unknown. It has been demonstrated that syphilis plays no rôle. Cultures from thrombi have always been sterile. There is undoubtedly a static, mechanical factor in the onset of the disease, for the lesions always occur in the lower extremities, and most frequently begin on the left side where venous stasis is most marked. Buerger states that "whatever may be the cause of the thrombosis, we feel inclined to take the view that, although the mechanical conditions that obtain in the lower extremities and the arteriosclerotic changes may be factors, some additional agent, be it toxic or otherwise, is at the same time responsible for the production of the periarteritis and thrombosis." It is a disease of *young adult life.* The patients are from twenty to forty years of age. It is a curious fact that most of the cases which have been seen have occurred in *Polish and Russian Jews.* However, these are not the only races affected. It is most frequently seen in the Free Dispensaries of large cities, where the cases are abundant. On account of the comparative youth of the subjects the disease has been called presenile, or juvenile gangrene.

Symptomatology.—Buerger's description is worth quoting in full: "The patients complain of indefinite pains in the foot, in the calf of the leg, or in the toes, and particularly of a sense of numbness or coldness whenever the weather is unfavorable. Upon examination we see that one or both feet are markedly blanched, almost cadaveric in appearance, cold to the touch, and that neither the dorsalis pedis nor the posterior tibial artery pulsates. When the foot becomes warm some color gradually returns. Some patients complain of rheumatic pains in the leg, others are able to walk only a short distance before the advent of paroxysmal, shooting, cramp-like pains in the calf of the leg makes it imperative for them to stop short. Some of these cases show the typical symptoms of intermittent claudication. After months—or, in some cases, even years—have elapsed, trophic disturbances make their appearance. It is at this stage that another rather unique symptom makes its appearance: one which gives the foot the appearance typical of erythromelalgia. When the foot is in the pendant position there is a bright red blush in the toes in the anterior part of the foot. This comes on rather rapidly, extending in some cases to the ankle or slightly above. Soon a blister, hemorrhagic bleb, or ulcer develops near the tip of one of the toes, usually the big toe, frequently under the nail, and when this condition ensues the local pain becomes intense. Such trophic disturbances may at times make little progress and last for months; sometimes, however, the skin in the neighborhood shows cyanotic discoloration, and dry gangrene of the whole toe is an early issue. Even before the gangrene, at the ulcerative stage, amputation may become imperative because of the intensity of the pain. The left leg is usually the first to become affected, although both limbs may show vascular disturbances almost simultaneously, and, when such is the case, the trophic changes, the ischemia, or the reddening, may give rise to a symptom-complex, often diagnosed as Raynaud's disease. In brief, after longer or shorter periods, characterized by pain, coldness of the feet, ischemia, intermittent claudication and erythromelalgic symptoms, evidences of trophic disturbances appear which finally pass over into a condition of dry gangrene."

Diagnosis.—From the description of the symptoms given above, thrombo-angiitis obliterans has to be differentiated from arteriosclerotic gangrene, from Raynaud's disease, and from erythromelalgia. If it is recalled that the condition appears in the lower extremities of young adults, there should be no difficulty. In erythromelalgia the arteries throb and the veins are prominent. Just the reverse is found in thrombo-angiitis obliterans.

Complications and Sequelæ.—Gangrene, the most serious complication, is in reality a part of the later stages of the disease. No sequelæ have been described.

Treatment.—In a disease in which occlusion of blood-vessels is the essential lesion, there is little that can be done to cure the actual process and to establish the lumina of the vessels so that the parts will receive their blood supply.

The pain is the most distressing symptom. This may be alleviated by **hot dry applications** and by **elevating the lower extremities.** Occasionally the so-called coal-tar derivatives, **antipyrin, phenacetin,** etc., may be used in 10 grain (0.65 gram) doses. The new muscle-spasm sedative drug, **benzyl-benzoate,** in doses of from 1 to 2 drams (4 to 8 c.c.), may be given. It may be necessary to administer **codein** or **morphin** for relief of pain. Intravenous injections of hypertonic **saline solution** have been extravagantly recommended. It is **doubtful** whether any good has resulted. The unsuccessful cases are not reported in the literature on the subject; however, the author knows of several. The saline is used in about 1 per cent. strength, and given twice daily quite warm. The amount varies. Some give 50 c.c. (or about 2 fluid ounces) and others give 200 c.c. (or about 7 fluid ounces) at one injection.

A **warm climate** is distinctly beneficial. Cold increases the discomfort and pain. The dry climate of the southwest, lower California, or Florida is helpful; however, this has little real curative value. **Static electricity** and **electric light baths** with mild heat have been used. When gangrene sets in, **amputation** affords the only relief. The amputation should be performed above the area of loss of arterial pulsation. Frequently the whole lower leg, including the knee, has to be sacrificed.

Prognosis.—The disease is not necessarily fatal. Neglected gangrene may eventually prove fatal, but since the gangrene is of the dry type, this is not as apt to prove fatal as if it were of the moist type. The disease may last for years without the occurrence of gangrene.

Pathology.—The gross lesions show grayish material in the lumen of the arteries, with occasional pin-point channels cut in cross section. In younger lesions, the clot is softer, and more pinkish. Still more recent lesions resemble the ordinary soft, red thrombus. The whole anterior tibial artery may be involved, including the dorsalis hallucis. The lesion may extend upward into the vessels of the thigh and suddenly cease at a branching of the vessel. Veins as well as arteries are affected. In the lower leg the posterior tibial veins are apt to suffer more than the anterior tibial. Together with the lesion of occlusion, there are periarteritis and arteriosclerotic changes. Only in the younger cases is arteriosclerosis absent. The periarteritis may be so extensive as to involve the structures immediately surrounding the artery, and the accompanying veins and nerve (if present) may be imbedded in a fibrous cord, difficult to dissect into its component parts.

Histologically the lesions may be divided into two main stages, (1) the healed or organized stage, and (2) the acute or incipient stage of thrombosis.

HEALED STAGE.—The thrombotic tissue is seen to be composed of connective tissue with sinuses of varying size and shape here and there. No elastic tissue is seen except a very small amount concentrically placed about the newly-formed vessels. "The termination of the occluding tissue in arteries and veins is often seen in the form of a rounded, convex projection pointing upward (cephalad) and lying in a practically healthy vessel-wall."

THE ACUTE OR SPECIFIC LESION.—This is characteristic, and a diagnosis is possible on the basis of examination of a portion of recently affected artery or vein. An inflammatory process involving all the coats of the vessel is apparently the early lesion. Polynuclear leukocytes are found, and the clot is red. At the periphery of the clot collections of leukocytes are found; these are followed by the appearance of foci comtaining giant-cells, endothelioid cells, or angioblasts and broken-down leukocytes. These foci undergo connective tissue replacement until only a fibrous nodule containing vessels and some pigment is left. Elsewhere the organization of the thrombosing clot is similar to that found in other conditions in which thrombosis occurs.

SYPHILITIC ARTERIOSCLEROSIS (ARTERITIS)

Syphilis is one of the few etiological factors which we feel reasonably sure does produce more or less extensive vascular change. The spirochetes have been found in the coats of the vessels, and in minute gummata in the vessels; according to Warthin, they are also numerous in the heart-muscle, in cases of syphilis.

There can be no doubt that the arterial tissue in the progeny of syphilitics is liable to early degeneration. Some maintain that all juvenile arteriosclerosis is due to hereditary syphilis. The superficial arteries are uniformly thickened by fibrous tissue; they are less elastic than normally, and appear to be actually smaller than the normal. The general under-development seen in many children of syphilitic parents may be the result of poor blood supply to the organs through the narrowed inelastic vessels.

In the acquired form, syphilis attacks the media of the artery. There is necrosis, fracture, and apparent solution of the elastic fibers. Small round-cells accumulate around the lesion. The adventitia of the vasa vasorum shows round-cell infiltration. The rapidly necrosed area in the media either becomes scar tissue or it is soon stretched by the blood-pressure, and a small aneurysm results. In the vessels of the brain these small aneurysms are quite common. Rupture of the vessels is not unusual. The cerebral arteries have been found to be the site of numerous small aneurysms when all the other arteries of the body appeared to be normal. Cerebral hemorrhage in a young person who has a normal blood-pressure is always due primarily to syphilis, unless different causes are found. The author has seen a number of such cases at autopsy. They are not uncommon in the large hospitals. Other lesions produced in the arteries by syphilis are aortitis and aneurysm.

SYPHILITIC AORTITIS

Definition.—This disease usually attacks the ascending portion of the aorta, is due to syphilis, and is characterized by dilatation of the arch and by aneurysmal formation accompanied by attacks of pain, dyspnea and palpitation.

Etiology.—The disease is caused in all cases by the localization of the *Spirochæta pallida* in the coats of the aorta. Although cases have been reported during the eruptive stage of syphilis, the average latent period is about sixteen years. Therefore, the disease is most frequently seen in the late secondary or tertiary stages at a time when no clinical manifestations are present. The spirochetes have been demonstrated in the artery. The disease is also found in cases of *congenital syphilis.* Longcope's youngest patient was a negro woman twenty-two years of age, his oldest, a man of sixty-eight years.

The majority of the cases occur before the age of fifty. About half occur between the ages of twenty and forty. Males are more often affected than females, the proportion being about three or four to one. The *negro race* is especially prone to the disease.

Symptomatology.—Syphilitic aortitis may be found at autopsy in cases in which there were no manifestations of its presence during life. There may be only a feeling of oppression beneath the sternum, or the patient may experience actual pain. The typical symptoms of the acute aortitis are pain, dyspnea, palpitation and tachycardia. The onset of the symptoms is apt to be paroxysmal. The patient may suddenly experience acute, oppressive pain beneath the sternum. This is accompanied by the most agonizing dyspnea. The patient sits up in bed, struggles for breath, waves his arms about, and becomes cyanotic. The heart becomes rapid and the blood-pressure rises rapidly. During the paroxysm the lungs are full of piping and mucous râles. The attack ceases more or less suddenly and is followed by a rapid subsidence of the lung signs and by a decline in the systolic blood-pressure. There is usually expectoration of bloody mucus. There may be several attacks daily, or these attacks may occur once a day or even less often. They are apt to be precipitated by exertion. At times there is the sensation of impending death, so characteristic of the attack of angina pectoris. The pain may also radiate toward the left shoulder and down the left arm, producing numbness.

The dyspnea is of the expiratory type. There is evidently spasm of the bronchial circular musculature in the terminal bronchioles. As a rule, the paroxysms end suddenly, leaving the patient quite exhausted.

PHYSICAL FINDINGS.—In the beginning of the process in the aorta there is no dilatation and no evidence of change which can be detected by physical methods. When the aorta has become weakened so that dilatation results, there is dulness beneath the manubrium; bronchial or tubular breathing may be heard with the stethoscope. There is often abnormal pulsation in the subclavian and carotid arteries, not infrequently accompanied by visible pulsations in the sternal notch at the base of the neck. Palpation reveals a distinct impulse.

The most important and probably the surest method of determining dilatation of the aorta is by the use of the *x*-ray, both with the fluoroscope and the teleroentgenograph. One should supplement the other. Occasionally a plate will show a shadow resembling a dilatation. If this does not pulsate under the fluoroscope, it is evident that it cannot be due to a dilated aorta. Teleroentgenograms should be made in order to minimize the distortion of the shadows. At two meters the rays are practically parallel and the true size of the aorta can be ascertained.

In the cases in which the pathological process has invaded the aortic valves and insufficiency of the valves has resulted, the usual enlargement of the heart will be found with the characteristic murmurs.

Frequently there is a loud aortic systolic murmur, which is caused by the passage of the blood through a normal-sized ring, over thickened valves, into a dilated ascending arch. In some cases, the aortic ring actually becomes slightly dilated, and produces the results of insufficiency of the valves, without actual disease of the valves being present.

During an acute attack, accessory signs may appear. Mucous and piping râles may be noted in a hyperresonant chest. The blood-pressure may show a sharp systolic rise. The presence of fever sometimes proves quite puzzling. The temperature may rise as high as 101° F. (38.33° C.) and may be either irregular or constant. The leukocyte count is not increased. The differential count may show an increase in the mononuclear elements, particularly in the small and large lymphocytes. Finally, the complement-fixation reaction may help to determine the syphilitic nature of the disease. A number of studies are now available which conclusively show the relationship between apparently non-infectious dilatation of the aorta, aortic insufficiency in persons past forty years with no history of rheumatism, aneurysm, and the Wassermann reaction. Thus, in 1908, Citron reported positive Wassermann reactions occurring in 62.6 per cent. of 16 cases of aortic insufficiency. Many have confirmed this relationship. In 1910 Longcope found 35 (74.4 per cent.) positive Wassermann reactions among 47 cases of aortic insufficiency. In a considerable number of cases studied the percentage of positive Wassermann tests in general cardiovascular diseases ranges from 25 to 68 per cent.; in aortic insufficiency, uncomplicated by mitral disease, from 75 to 100 per cent.; in aneurysm, from 85 to 95 per cent.; in aortic disease in general, including aneurysm, dilatation and angina pectoris, from 75 to 88 per cent.

When the process involves the cusps of the aortic valves—as it very frequently does—the valves become thickened, shortened and incapable of closing the aortic orifice. Regurgitation of blood takes place during diastole, and gradually dilatation and hypertrophy of the left ventricle appear. The signs which are present are the ones usually found in aortic regurgitation.

It must be emphasized that syphilitic aortitis not only produces lesions in the aorta, but is also a frequent cause of aortic insufficiency in cases in which no history of acute rheumatic fever or other serious infectious disease can be obtained. *Aortic insufficiency in a person of forty or over is due to syphilis unless proved to be due to some other cause.* If this sweeping statement is kept in mind, fewer mistakes will be made in determining the etiology.

Diagnosis.—The condition must be differentiated from angina pectoris, thrombosis of the coronary arteries, rheumatic or other infectious aortic regurgitation, and aneurysm of the ascending arch. As such patients frequently have attacks of *angina pectoris,* it is not easy to exclude the latter disease. However, the anginal attacks are usually momentary; there is no great respiratory distress such as is seen in attacks of syphilitic aortitis. Occasionally, patients suffering from syphilitic aortitis drop dead during an anginal attack. The Wassermann reaction and the *x*-ray examination, together with the physical signs of dilatation of the aorta, will usually establish the diagnosis. Occasionally, no dilatation of the aorta can be distinguished, even by means of the *x*-ray.

In *thrombosis* a sudden agonizing pain appears, usually in the upper abdomen, and there are signs of collapse. Electrocardiographic tracings are helpful in establishing a diagnosis. The inversion of the T-wave is characteristic.

Attacks of paroxysmal pain, dyspnea and palpitation are unknown in aortic insufficiency of infectious origin. The case history and the Wassermann reaction will establish the diagnosis.

In *aneurysm,* the pain, if present at all, is constant, and of a dull, boring character. Other signs, such as dilatation of the pupil, irregularity of the pulse in the wrists, change in the voice, tracheal tugging, etc., aid in establishing the diagnosis.

In cases in which there is a history of *acute rheumatic fever* with aortic insufficiency and a positive Wassermann reaction, it may be impossible to determine the etiology of the cardiac lesion. Furthermore, acute endocarditis may be superimposed upon syphilitic involvement of the aortic valves.

Treatment.—The treatment of such cases naturally varies with the stage of the disease. In cases of acute aortitis, in which the aortic valves have not yet been damaged, intensive antisyphilitic treatment should be instituted according to the accepted methods. It is still a matter of opinion whether **arsphenamin** or **neo-arsphenamin** should be given in small and frequent doses every second or third day, or whether the doses should be large and given at intervals of a week or ten days. The author prefers the less frequent doses combined with intramuscular injections of **mercury** or with intravenous injections of mercury in the form of the albuminate in conjunction with **potassium iodid** in doses rapidly increasing to the point of saturation. Five or six injections of arsphenamin or neo-arsphenamin with from twenty to thirty injections of mercury constitute one course of treatment. Nothing further should be given for a period of time varying from several weeks to two months. The course should then be repeated. Wassermann tests should be made before and after every course. It is not always possible to produce a negative test. Here one must be guided by judgment, based upon the patient's condition. It would not seem to be good practice to continue the specific treatment indefinitely when a negative Wassermann reaction cannot be obtained.

Where the case is an old one and a lesion of the aortic valves is present, the author believes that treatment should be very carefully given. It has been his experience that more harm than good results from giving intensive treatment with arsphenamin or neo-arsphenamin. Should symptoms such as pain and a tendency to paroxysms be present, one should use these drugs tentatively. However, the author considers that he has obtained the best results with mercury and potassium iodid. When decompensation sets in, it is combated as usual, irrespective of the cause of the cardiac lesion. For the acute paroxysm, hypodermics of **morphin** (1/4 to 1/2 grain, or 0.0162 to 0.0324 gram), combined with **nitroglycerin** (1/100 grain, or 0.0065 gram), should be given.

Pathology.—Anyone who is at all familiar with the gross lesions of syphilitic aortitis has no great difficulty in recognizing the characteristic appearance of the aorta. Usually the lesions do not extend beyond the mouths of the great vessels, and the scarred and dilated ascending arch is sharply demarcated from the smooth aorta beyond. The earliest recognizable lesion is a pale gray, elevated translucent, irregular patch measuring five or more centimeters in diameter. On section, the elevated area is found to be grayish; deeper in the portion corresponding to the media there are yellowish, opaque streaks running lengthwise. The lesion may surround the vessel. Later, scarring takes place, and the areas are depressed, whitish, and have a crinkly appearance which has been likened to that of parchment. Here and there may be very thin areas the size of beads, which represent aneurysmal dilatations. The whole aorta becomes dilated and more or less rigid, due to loss of the elastic fibers. The process may extend around the orifices of the great vessels and constrict them. Only rarely is calcification found. In the extension of the process toward the root of the aorta, the valves become affected. The free edges are thickened and curled. The sinuses of Valsalva are often dilatated, or only one is so markedly affected that the ring is actually dilated. The orifices of the coronary arteries are often constricted, but the process rarely extends into the arteries.

With the involvement of the aortic valves, insufficiency in their function results, with consequent changes in the left ventricle. All three of the coats are seen microscopically to be involved, although the process is believed to begin in the media. There is accumulation of round-cells in the adventitia around the vasa vasorum. In the media the elastic fibers appear to have been dissolved, and there is necrosis with round-cell infiltration. In the intima there is an accumulation of cells, forming an actual projection into the lumen of the aorta. The areas of necrosis in the media may be extensive, and resemble true gummata. Aneurysmal dilatations are found in these weakened places. The late stages reveal scar-tissue, in which are embedded fragments of elastic tissues.

ANEURYSM

Definition.—An aneurysm is a local dilatation or expansion of the coats of an artery, which produces a bulging upon the external surface of the vessel. Aneurysms vary in size from minute bulgings on small arteries to huge tumors along the course of the thoracic aorta. Several forms of aneurysms are described. The most usual and convenient classification follows:

1. True aneurysm.
    - *(a)* Sacculated.
    - *(b)* Fusiform.
2. Dissecting aneurysm.
3. False aneurysm.
4. Arteriovenous aneurysm.
5. Cirsoid aneurysm.

True Aneurysm.—In this variety one or more of the coats of the artery form the walls of the aneurysm. Usually at least two of the coats are found, the intima and adventitia. Portions of the media in such cases may be recognized, but this coat is usually so destroyed that it is not easily found, even after careful dissection.

Sacculated Aneurysm.—The sacculated aneurysm occurs as a definite tumor bulging out from the artery wall and connecting with the lumen of the artery by a small opening. The aneurysm grows by the accretion and coagulation of blood within the tumorous sac. This forms a solid mass; frequently the laminated clots fill the sac; the oldest clots are found farthest away from the vessel, where the color has changed to a whitish or brownish tint.

"Owing to the large area and great thickness of the fibrin deposited, and to the fact that the intimal endothelium is in most places still intact, there is little entrance of fibroblasts into the clot, and little organization goes on. The aneurysmal clot is, therefore, not converted into a solid mass of connective tissue as in endarteritis or thrombo-angiitis obliterans, but remains simply laminated fibrin. Deposits of calcium salts sometimes occur upon them, however, and tend to convert the obliterated aneurysm into a solid tumor'' (Hirschfelder).

Fusiform Aneurysm.—Dilatation of the arch of the aorta is very common. It is always associated with increased pulse-pressure, and in aortic insufficiency, for example, it may be very marked. There is only a degree of difference between diffuse dilatation and fusiform aneurysm, for the latter is merely a diffuse dilatation of a portion of the arch. All the coats are involved.

DISSECTING ANEURYSM.—In this form the blood extravasates between the coats of the artery The extravasated blood may completely surround the artery, forming a tube within a tube, and may break again at some lower point into the lumen of the artery.

FALSE ANEURYSM.—This is a periarterial extravasation of blood following puncture or rupture of all the coats of the artery.

ARTERIOVENOUS ANEURYSM.—Following wounds through both an artery and its accompanying vein, there is a communication between artery and vein either directly—an aneurysmal varix—or through a sac which is formed—a varicose aneurysm. This is strictly a surgical condition.

CIRSOID ANEURYSM.—This is a soft tumor composed of a large number of tortuous arteries which are branches of a common stem-artery. This is also known as telangioma. It is rare and occurs on the scalp.

Etiology.—The aneurysmal bulging begins in a rupture of one of the coats of the artery, usually the media. This rupture is caused by a weakened media plus the pressure in the artery due to cardiac systole. Theoretically, the weakness of the media may be caused by arteriosclerotic lesions, by violence, or by the action of the toxins of many infectious diseases. Such primary lesions as these occasionally occur. Practically the most important single exciting cause is *syphilis,* which attacks the ascending aorta in a particular manner. (See Syphilitic Aortitis.) Long before the discovery of the complement-fixation test for syphilis, clinicians and pathologists thought that all aneurysms in persons under thirty years of age were caused primarily by syphilis. In fact the very general employment of the Wassermann reaction has demonstrated that a high percentage of aneurysms at all ages is due to syphilitic infection.

Occasionally, as the result of a violent *strain* in a diseased aorta, the intima alone may rupture, or the tear may extend into the media and the blood may force its way between the coats of the aorta. *Trauma,* such as a stab-wound, may produce an extravasation of the blood, which may form a large hematoma beside or surrounding the blood-vessel.

Another important factor in the production of aneurysm is the strain on the blood-vessel which is produced by the *heart-beat;* without this aneurysm would scarcely be possible. At every systole the aorta is forcibly dilated. Any weak spot in its wall will therefore tend to bulge more than the normal vessel-wall. Whenever there is heavy muscular exertion involving great strain, the blood-pressure is much increased and the aorta is more violently stretched.

Numerous case histories lend support to this conception. Sudden onset at a definite time during a strain is frequently elicited in the history. In the case here illustrated the patient was positive that his first symptom, pain coming on suddenly, was the result of a jail punishment which consisted in his being strung up by his thumbs until his toes just touched the ground.

What Adami calls "strain hypertrophy of the aorta" probably has a place in the etiology. In this condition constant *hypertension* mechanically stretches the blood-vessel, so that here and there rupture of the elastic tissue occurs, the intima is stretched, and an accumulation of cells results. This usually leads to a diffuse dilation of the arch, so that an aorta which normally measures from 5 to 5½ cm. in diameter may be 7 or 9 cm. in diameter.

An occasional cause of aneurysms in the smaller arteries is the plugging of the blood-vessel by *septic emboli.* This may occur at the bifurcation of a vessel, and the embolus may lie astride of the point of bifurcation and partially or completely plug both branches of the vessel. Softening of the walls follows. Rupture may occur into the surrounding tissue, or a weakening of the coats may result, so that the vessel may bulge from the internal pressure. This embolic, or mycotic, type of aneurysm is rare.

Aneurysms are found at all ages; children are not exempt, but the ages of greatest incidence are those in which bodily activity is greatest. Hence most aneurysms are found in *men* between the ages of *thirty and fifty.*

Alcohol, tobacco, lead and other tissue poisons, *gout, diabetes, rheumatism,* are *not* important factors in aneurysm. Acute articular rheumatism, in its tendency to attack the heart-valves, and occasionally the first part of the ascending aorta, is the most frequent of all the infectious diseases which contribute to the etiology.

Heredity plays no rôle except in the cases of aneurysms in children, inasmuch as hereditary syphilis is not infrequently present in the child.

Finally, aneurysms may be formed by the weakening of the blood-vessel due to an extension of a neighboring *inflammation;* the coats of the vessel thereby become softened and the pressure from within produces a bulging at the weak spot in the vessel. *Men* are much more prone to aneurysms than women, the proportion being about 5 to 1; and the *negro race* is especially affected, due to the frequency with which negroes contract syphilis, and to the character of their work as stevedores, laborers, miners, etc.

Any artery may be affected, but the thoracic aorta and the popliteal artery lead in the incidence of aneurysm. Thus, in a series of 530 cases (Crisp) the arteries were affected as follows:

Thoracic aorta	175
Popliteal artery	137
Femoral artery	66
Abdominal aorta	59
Carotid artery	25
Subclavian artery	23
Axillary artery	18
External iliac artery	9
Cerebral artery	7
Common iliac artery	2
Posterior tibial artery	2
Gluteal artery	2
Pulmonary artery	2
Brachial artery	1
Subscapular artery	1
Ophthalmic artery	1

Aneurysm may be multiple; two or more may occur along the aorta or along any artery.

Symptomatology.—It is convenient to divide aneurysms into those characterized (*a*) by signs, and (*b*) by symptoms. The former are for the most part found in the ascending arch, while the latter include the aneurysms of the transverse arch. The symptoms vary greatly. The growth of the aneurysm *per se* does not as a rule produce any symptoms. All of the distress of which the patient complains results from pressure of the aneurysm upon adjacent structures. An aneurysm which grows upward and to the right, or which bulges to the right from the ascending arch or to the left from the descending arch, may reach an enormous size, with little or no discomfort to the patient. On the contrary, a very small aneurysm, involving the transverse arch or the first part of the descending arch, may press upon the neighboring structures to such an extent that it gives evidence of its presence by symptoms long before objective signs can be elicited.

In probably one-half of the cases an aneurysm near the sinus of Valsalva is free from symptoms and gives evidence of its presence only when death suddenly occurs due to perforation into the pericardial sac. Dissecting aneurysms have been known to rupture into the pericardial sac. Even young children are not altogether exempt. Death may not be sudden. The patient may live for several hours after rupture. In many cases the heart becomes dilated and hypertrophied through the insufficiency of the aortic valves, which may be involved in the syphilitic aortitis; or the aorta just above the valve may become so stretched by the growth of the aneurysm that a dilatation of the ring occurs and a relative insufficiency results. Signs of heart-failure may, at any time, complicate the aneurysm. Indeed, death from heart-failure may be due primarily to an aneurysm which presented no symptoms, and which was overlooked, because, when the patient came under observation, the cardiac decompensation signs, cyanosis, edema of lungs, edema of the legs, enlarged liver, irregular pulse, etc., dominated the picture. Syphilis, as shown by Warthin and others, attacks not only the aorta but the heart itself, inducing widespread necrosis, which leaves a scar formation when healed. Hence the heart is in a weakened state and prone to break down upon comparatively light strain.

Aneurysms occur for the most part in robust, full-blooded individuals. They may advance rapidly in size and cause loss of appetite, loss of weight, interference with sleep, and emaciation. Bronchopneumonia may terminate the patient's misery, or acute compression of the trachea or of the esophagus may cause death. Of the special symptoms, the most constant is *pain,* which may be either of a dull, boring, constant character or paroxysmal. There may be only a feeling of weight or oppression beneath the sternum. Anginal attacks may occur, the pain radiating down the right or the left arm. Pain in the chest is such a constant symptom that it should arouse suspicion of aneurysm, when the pain cannot certainly be accounted for by some obvious condition.

When the aneurysm involves the descending portion of the arch, the pain is apt to be constant and excruciating, due to the erosion of one or more vertebræ and the consequent pressure and inflammation around the roots of the nerves. Often the pain is referred to the front of the chest or to the upper part of the abdomen in the distribution of the nerves. Pain may be the only symptom of the disease and may simulate the pain of gastric crises in tabes dorsalis.

Shortness of breath on exertion, similar to that produced by cardiac disease, may be the initial symptom, or it may accompany the pain. The dyspnea is frequently manifested only upon lying down at night. Other symptoms involve special structures which are pressed upon by the tumor.

On the left side the recurrent laryngeal nerve loops around the transverse portion of the arch of the aorta. On the right side the nerve loops around the subclavian artery. The high position of the right nerve protects it to a great extent from injury. However, when an aneurysm involves the first part of the transverse arch and the innominate artery, the nerve is involved in the sac and symptoms characteristic of pressure are produced. On the left side the nerve is exposed to injury much more frequently, due to the greater incidence of aneurysm of the transverse arch. Irritation of the nerve may produce spasm of the larynx, and interference with swallowing; it also gives rise to a peculiar cough described as "brassy," or as the "goose" cough. It is so distinctive that one knowing the characteristics of the cough can frequently detect the case of aneurysm among the patients in a large ward.

The voice is husky, and when the nerve is destroyed, the vocal cord is completely paralyzed and lies in the so-called cadaveric position. The right cord may then be brought across the median line in an effort to produce phonation. However, in such cases huskiness is so great that only whispering is possible. While the left cord is the one commonly paralyzed, it must not be forgotten that the right cord, for reasons given above, may be as completely paralyzed and may produce the same symptoms as paralysis of the left cord.

The phrenic nerves lie just back of the pericardial sac, but are not often involved in aneurysm. Should they be irritated, hiccough or spasm of the diaphragm may be present. Irritation or paralysis of the sympathetic fibers at the root of the neck may produce dilatation or contraction of the pupil; this usually occurs on the left side. The pupillary change may also be due to changes in the blood supply. Usually there is slight dilatation. The response to light is present. As syphilis is also responsible for irregular pupils, the light reflex will differentiate the cause of the irregularity.

Difficulty in swallowing may be due to a transient spasm caused by the irritation of the recurrent laryngeal nerve, or it may be persistent when the aneurysm actually presses upon the esophagus. Usually the patient thinks he feels a lump in his throat, and solid food may seem to stick momentarily. At autopsy, the esophagus has been found to be stretched to twice its width and firmly adherent to the aneurysmal sac; yet during life the condition had produced no symptoms. Everything depends upon the manner in which the tube is compressed. Even in large aneurysms the esophagus is merely pushed aside and not compressed against the vertebræ or ribs. It is well to bear in mind the fact that apparent strictures of the esophagus may be due to the pressure of an aneurysm.

Cough is a very common and often a most distressing symptom. It is dry and hacking, and may be so persistent that the patient has no rest day or night. Such a cough is usually due to the pressure of the aneurysm upon the trachea, which is often eroded; ulceration of the mucous membrane has also been found. Dyspnea may be due to the actual narrowing of the air inlet. One or the other main branches may also be compressed; cough is likewise the chief symptom. Often the patient can tell from which side the cough arises. Imperfect aëration leads to the collapse of portions of a lung, or, in rare cases, to the collapse of a whole lung.

When the aneurysm is large, it may actually compress the lung and cause collapse with eventual fibrosis. While a certain amount of collapse occurs in all aneurysms of the descending arch and thoracic aorta, it is rarely sufficient to cause symptoms.

Interesting collateral circulation is frequently caused by the pressure of the aneurysm upon the veins. The space through which the structures above the heart pass is small and many large vessels are found there. Almost any tumor will produce some compression of the veins. Rarely is one of the large veins, for example, the superior vena cava, obliterated, but the subclavian and jugular veins, particularly the left one, are often compressed to such a degree that the blood has to find its way from the head and arm to the inferior vena cava through the anastomosis of the mammary with the epigastric veins. One side of the chest may show dilated and tortuous veins with the current flowing from above downward. Fullness in one side of the head may be complained of, and there may be slight edema of the arm.

PHYSICAL FINDINGS.—*Inspection.*—The physician who trains his eye so that he sees with his cerebral cortex and not alone with his retina will make many diagnoses of aneurysm by inspection. This method should never be neglected. It is of prime importance in diagnosis. The patient should be stripped to the waist and placed in a good light. Osler often called attention to the number of aneurysms which were unrecognized because of the examiner's habit of pushing the shirt up under the chin. The most important area of the chest is thereby either covered, or has a shadow thrown over it.

The area from the base of the heart to the sternal notch is the region in which most signs are found. Visible, expansile pulsations, synchronous with the systole of the heart, are to be anticipated. The characteristic of the aneurysmal tumor is expansibility. A pseudo-expansile pulsation is often seen in the course of the abdominal aorta when a solid tumor overlies that vessel. The first and second interspaces to the right or to the left of the sternum are the commonest sites of abnormal visible pulsation. If one looks down the patient's back, he may see pulsation near the lower angle of the scapulæ.

This pulsation must not be confused with that of the conus of the right ventricle which is found in the second left interspace. This is common in children and in thin-chested persons. Throbbing of the aorta in anemic states, in aortic insufficiency, and in Graves' disease may simulate aneurysm. Occasionally a pleural effusion may so dislocate the heart that there are pulsations in unusual places. If one bears these in mind and exercises reasonable care, there should be no difficulty in diagnosis.

The slight inequality of the pupils in connection with the reaction to light often directs attention at once to some intrathoracic trouble. Dilated veins on one side, abnormal pulsation of the vessels of one side of the neck, and edema of the arm or upper chest, are easily seen if a careful inspection is made. A diagnosis of aneurysm can be made in many cases by inspection alone. Other methods of examination are only confirmatory.

Palpation.—A visible pulsation can usually be felt. There is a distinct push on the palpating finger. A thrill systolic in time may be felt, and the closing of the aortic valve is felt as a distinct thump, the diastolic shock.

In the abdomen it is often very difficult to determine whether or not a pulsating tumor is expansile. Palpation with both hands, one on each side of the tumor, will help to determine the question. The pulsation must be expansile.

(*a*) *Peripheral Arteries.*—When an aneurysm involves the arch so that the orifices of one of the three great branches are included there may be definite palpable changes in the pulse-waves of the carotids or radials on the two sides. Both delay and decrease in size of the pulse-wave are found separately or together. The common practice of feeling one radial when making an examination is to be deprecated. The practice of grasping both radials, one with each hand, would save much confusion in diagnosis. Conditions other than aneurysm may produce changes in the radials or carotids, but these will be more easily eliminated when attention is directed toward the possibility of aneurysm.

(*b*) *Tracheal Tug.*—This is a sign which was described by Oliver in 1878. It is due to the adhesion of the sac to the trachea; this in turn transmits the impulse to the trachea. It is one of those accessory signs described in so many diseases which has absolutely no bearing on the diagnosis. To elicit this sign the examiner directs the patient to incline his head slightly forward. The cricoid cartilage is then firmly grasped by the examiner, or the finger is placed in the cricoid notch, and an upward pull is made. At each systole, if the sign is present, a tug may be felt. It is interesting, but has little or no diagnostic value.

Blood-pressure Examination.—The blood-pressure is usually equal in both brachial arteries. In aneurysm there is often a difference of from 10 mm. to 20 mm. in the systolic pressure on the two sides. The diastolic pressure is not affected. Here again it is of distinct value to take the blood-pressure on both arms at the first examination.

Percussion.—Many aneurysms of the arch are so situated that they modify the normal clear percussion note over the chest and back. Normally, the whole upper chest above the third rib, including the mediastinum, has a resonant percussion note. A tumor of moderate size may impair the note; if the tumor is large, it may cause a flat sound below and on both sides of the manubrium for a variable distance. The percussion stroke should be exceedingly light, so that the smallest possible resonating area may be set to vibrating. The dulness due to aneurysm of the arch is continuous with the cardiac dulness. In the back there may be a perceptible change of percussion note over a large aneurysm. The pitch of the note will depend upon the amount of lung-tissue which lies between the tumor and the chest-wall.

Auscultation.—Various sounds are heard over aneurysms. Over the aortic area there is often a long systolic murmur of a rough rasping character, transmitted far along the branches. When aortic valves are incompetent, a low-pitched diastolic murmur is heard. The palpable diastolic shock is heard as a ringing sound over the aorta. At times there may be a continuous hum, "bruit de diable," and again no sound will be heard at all.

A small aneurysm in the anterior mediastinum may give a bronchial or tubular quality to the respiratory murmur when the stethoscope is placed on the skin over the manubrium. Tubular breathing can practically always be heard in aneurysm of the arch, but often the loud heart and vessel sounds so dominate the auscultatory phenomena that the breath sounds are obscured. The author has found that auscultation over the manubrium is a valuable help in diagnosing tumor masses in the mediastinum.

X-ray Examination.—The study of aneurysm is not complete unless the fluoroscope and radiograph are used. This is not an implication that one cannot make a diagnosis of aneurysm without the ray; diagnoses were made successfully long before Crookes discovered the kathode emanation and before Roentgen made the *x*-rays practicable in diagnosis. However, in every case of suspected aneurysm a careful *x*-ray examination should be made. Only in this way can many aneurysms be surely discovered. The fluoroscope is of more diagnostic value than the plate. The latter only reveals a tumor, which may be an aneurysm. But with the fluoroscope one can see the expansile pulsation in a tumor above the heart. A healed sacculated aneurysm full of solid laminated clot would behave like any solid tumor. In such a case the presence of enlarged glands in the axillæ or neck would assist in determining whether the picture was one of solid aneurysm or of mediastinal tumor. In order to obtain the true size of an aneurysm, teleoroentgenograms should be made. The ordinary plate taken with the tube at a distance of from twenty-four to thirty inches increases the size and distorts the shadows of the chest organs.

Development of the Aneurysm.—An aneurysm once formed grows, as a rule, toward the regions of least resistance. In the course of its growth it may come in contact with the bony structures or with the softer parts of the body. It is not uncommon for the aneurysm to erode the ribs or sternum and to point toward the surface of the skin. The erosion of the ribs and sternum is usually painless. However, aneurysms of the thoracic aorta may erode the vertebræ and give rise to great pain. The trachea, bronchi, and esophagus may also be eroded, and the aneurysm may bulge into the lumen of any of these structures. The direction which the aneurysm takes is to a large extent determined by its situation on the arch. Thus, aneurysms of the ascending arch point to the right and upward in the direction of the blood stream; those of the transverse arch point upward and backward; and those of the descending arch point upward and toward the left.

Rupture.—About one-half of all deaths from aneurysm of the arch are the result of more or less sudden rupture. This may occur through the chest when erosion has brought the sac just beneath the skin; or it may break into the pericardial sac, the trachea, the bronchus, the esophagus, a large vein, etc. The aneurysm in the abdominal aorta rarely ruptures into the duodenum. A case with autopsy findings was reported in which the abdominal aneurysm in a previously healthy woman ruptured into the tissues of the retroperitoneum. There was sudden acute abdominal pain and collapse. The patient rallied temporarily and died twelve hours later of further hemorrhage.

Death may be sudden, or it may be delayed for several hours. There are several cases on record of rupture into the pleural cavity in which the patient survived one or two days. Oozing of blood from an aneurysm which has eroded the ribs or sternum is not at all uncommon. The skin becomes discolored and finally ulcerates. Oozing begins through a fungus-like, spongy opening in the aneurysmal sac. It may continue for a number of days and cease spontaneously. Suddenly there may be a gush of blood, and the patient may die in a few minutes. High blood-pressure, resulting from strain, is often the determining cause in a rupture.

Diagnosis.—In spite of the number of symptoms and signs which may occur in aneurysm of the thoracic aorta, the diagnosis is often difficult. Substernal pain alone may be due to simple dilatation of the aorta and must not be confused with that of aneurysm. This latter is to be differentiated from (1) solid tumors of the mediastinum, (2) dilatation of the arch, (3) pulsating encapsulated empyema in the upper chest, (4) pulmonary tuberculosis, and (5) mitral stenosis.

If these conditions are borne in mind and it is remembered that the tumor must be expansile, mistakes may be avoided. In suspected cases the *x*-ray is invaluable. Occasionally an aneurysm is so far healed that it is more or less solid and does not expand at every cardiac beat. In such a case the smooth globular outline of the tumor and its close association with the aorta should be sufficient for diagnosis. Occasionally a tortuous subclavian artery or an enlarged jugular bulb may simulate aneurysm. These conditions should cause no great difficulty in diagnosis, if care is exercised in the examination.

Aneurysms of the arch are sometimes overlooked through carelessness in examination and failure to keep in mind the constant possibility of this condition. Careful percussion and auscultation over the manubrium in every case will prevent many errors. Aortic insufficiency is so frequently associated with aneurysms of the ascending arch that the aneurysm is apt to be submerged in evident cardiac lesion. Here, again, care is essential and the *x*-ray is a valuable aid.

Clinical Varieties.—DISSECTING ANEURYSM.—In this type of aneurysm there are no symptoms which are distinctive. In the great majority of cases the condition is found only at autopsy. Occasionally the aneurysm perforates and death results. In one such case in a girl twelve years old the aneurysm perforated into the pericardial sac. The aneurysm forms through a fracture of the intima and the media, in which event the blood works its way between the media and the adventitia. After a time, endothelium may form in the wall of the false channel.

ARTERIOVENOUS ANEURYSM.—Communication between an artery and a vein is not as uncommon in the peripheral arteries where perforating wounds, especially bullet wounds, can penetrate both artery and vein. In the late World War there were a number of such aneurysms; they were usually found between the femoral artery and the vein. The diagnosis is not difficult.

A much rarer situation is in the thorax between the aorta and superior vena cava. Death usually follows in a few hours, but the patient may survive and live for several months. The rupture is ushered in by sudden intense dyspnea, cyanosis of the face, and distention of the veins of the neck. A tense edema rapidly supervenes, and dilated veins quickly form over the thorax and end abruptly at the attachment of the diaphragm. Over the perforation site, which is naturally near the aortic cartilage, a thrill is usually felt, and on auscultation a continuous murmur is heard; this increases in intensity, at every systole. "Perforation into the *pulmonary artery* is attended by sudden and severe dyspnea, which is followed by cough and occasional blood-streaked sputum. A thrill over the pulmonic area is occasionally present. The most characteristic physical sign is a continuous, roaring murmur, with a systolic intensification; this is heard over the pulmonary area. Perforation of the pulmonary artery is not, as a rule, immediately fatal. A period of weeks or even months may elapse before death occurs" (Landis).

Aneurysm of the Abdominal Aorta.—Aneurysm of the abdominal aorta is not so common. At the Milwaukee County Hospital, not one case has been seen among the last 500 autopsies; in the wards, among the admissions of the last five years, 9,584 patients, not one case has been seen, although during this time there were 54 thoracic aneurysms. This type is said to constitute from 10 to 14 per cent. of all aneurysms. Pain is the prominent symptom. It may simulate the pain of gastric ulcer. Erosion of the spine is common. Under such circumstances the pain is constant and excruciating. Large doses of morphin do not cause it to cease, although they usually alleviate it to some extent. A patient with large eroding abdominal aneurysm is truly a pitiable sight.

Violent pulsation of the abdominal aorta is a frequent condition, particularly in neurotic persons. The shock may be so great as to jar the bed in which the patient is lying. The relaxation of the abdominal organs, the looseness of the retroperitoneal tissue, the low peripheral resistance, are probably all factors in producing the violent pulsation. Solid tumors, such as may occur in the stomach, may lie upon a bounding aorta and produce on inspection an appearance not unlike that of aneurysm. The most common seat of the aneurysm is around the celiac axis or near the branches leading to the kidneys.

The difficulty in diagnosing the aneurysm rests somewhat in its location high up behind the lesser peritoneal cavity. *Unless there is a tumor which can be grasped between the fingers of one or of both hands and felt to expand in all directions at every heart-beat,* one is not justified in making the diagnosis of aneurysm. No mistakes are made by adhering rigidly to that rule. It is surprising how difficult it is at times to decide whether or not the above criteria are fulfilled in any particular case.

The aneurysm may be fusiform, sacculated or dissecting. There may be a difference in the time of the femoral beats; the beats in both arteries may be delayed appreciably; or, if the aneurysm is large, it acts as a catch-basin for the pulse-wave and there is no femoral pulse, and the blood flows through in a constant stream propelled by the recoil of the large reservoir sac on the aorta.

Aneurysms of other Arteries.—Aneurysm of the ophthalmic artery or of the vertebral or basilar arteries is rarely found. The diagnosis is practically impossible. Aneurysms of the arteries of the arms and legs present no especial problems. They are largely of surgical interest. The commonest is aneurysm of the popliteal artery.

Treatment.—The medical aneurysms, so to speak, are in almost all cases the result of syphilitic aortitis, so that the prophylaxis of aneurysm is the prophylaxis of syphilis. If there is no syphilis, there is no aneurysm; or if syphilis is absolutely cured there is likewise no aneurysm. Therefore, in order to prevent the development of aneurysm, it is necessary to go back years in the life of the individual. Once the damage is done it is irreparable. Aneurysms may heal spontaneously by laminated clotting within the sac, but this is possible only in the case of those aneurysms in which there is a small opening and a large sac. There can be no spontaneous healing where the opening is large or where the aneurysm is fusiform in type.

General Measures.—Most patients suffering from an aneurysm present themselves on account of pain or cough or both. Cough mixtures are useless. The patient should be **put to bed**. This reduces the number of pulse-beats and lowers the blood-pressure. At the same time **potassium iodid** should be given twice or three times daily in doses of 15 grains (1 gram). The patient should be kept in bed several weeks and should be given a diet of about 10 calories to the pound weight of the patient.

In 1874, Tufnell revived the **rest and starvation** treatment. He gave ten ounces of solids and ten ounces of liquids daily for several weeks. The patient must maintain a **horizontal position,** not rising for anything. No water is allowed. Tufnell's diet formula follows:

Breakfast	Bread and butter.....	60 grams	(2 ounces)
	Milk	60 c.c.	(2 ounces)
Dinner	Meat	60–100 grams	(2–3½ ounces)
	Milk	75–125 c.c.	(2¾–4¼ ounces)
Supper	Bread	60 grams	(2 ounces)
	Milk	60 c.c.	(2 ounces)

This is exceedingly rigorous and of doubtful value. However, limitation of the diet is essential. **Calcium lactate** and **gelatin** injections have been given during this rest period with **doubtful** results. After the rest treatment, the patient should lead a very quiet life, throwing as little strain as possible upon his blood-vessels. The question naturally arises: should antisyphilitic treatment be given? In many cases the Wassermann blood-serum reaction is strongly positive. In such cases it seems rational to give intramuscularly from 0.06 to 0.12 gram (1 to 1.5 grains) of **mercury salicylate** weekly for five or six weeks. A period of rest should follow; then a further course should be given, and the intervals between treatments should be lengthened until the patient takes only one or two courses of treatment a year. The blood should be controlled by the Wassermann reaction, although it is not always possible to produce a negative reaction. The patient must be kept under observation, if possible, so that the symptoms can be controlled as they arise.

Arsphenamin and **neo-arsphenamin**, if given, should be carefully administered. It is advisable to commence treatment with small dosages, e.g., 0.3 gram (5 grains), so that the effect of the treatment can be studied. More harm than good may result from too intensive treatment. In some of those cases the Wassermann never becomes negative. Hence it is obviously futile to continue giving arsphenamin. Much judgment is required in treating such cases and no rules can be formulated.

Several years ago **wiring** of an aneurysm had quite a vogue. About ten feet of specially prepared coiled wire were introduced into the sac through a special needle. The free end was then connected to the anode of a galvanic battery. A pad under the patient's back was connected with the cathode terminal. A current of 10 milliampères was administered for thirty minutes. The current was then increased to 20 milliampères for ten minutes, if the patient could stand it. No constant results were obtained and the method seems to have fallen into disuse. It was applicable only to true sacculated aneurysms in which spontaneous clotting was favored. In a case at autopsy the author saw ten feet of wire coiled in the transverse arch directly in the blood stream.

In case the aneurysm is eroding the vertebræ and causing intense pain, symptomatic relief with **opiates** is all that can be accomplished. The fear of creating a morphin habit should not prevent the physician from relieving the actual pain. Abdominal aneurysms may be amenable to surgical treatment, but as a rule, they occur high up near the celiac axis and are inaccessible to surgical intervention.

Prognosis.—Aneurysms may reach a certain size and then become stationary; or in rare cases, they may heal spontaneously. For the great majority of cases, the course is from one to five years, although the aneurysms may remain stationary and be compatible with a fairly active life for twenty or even thirty years.

Rupture, either through the chest-wall after erosion or into some neighboring structure, is the most frequent mode of death. This has been discussed above. However, in about 45 per cent. of cases, death is due either to pressure upon important nerves and blood-vessels, or to changes which take place secondarily as a result of such pressure. Once the aneurysm begins, the usual course is progressive growth, slow or rapid, depending upon many circumstances.

Pathology.—Aneurysms may be produced by violent strain alone in an aorta already thinned and weakened by arteriosclerosis. It is exceedingly doubtful whether any sudden rise of pressure could rupture a normal artery. It has been demonstrated that the aorta will withstand a strain ten to twenty times greater than the normal systolic pressure, before rupturing. No such pressure could occur during life. Syphilitic aortitis precedes the formation of aneurysm in the great majority of cases. The lesion occurs first in the media when necrosis takes place; elastic fibers are dissolved and round-celled infiltration takes place. The intima proliferates and the adventitial vessels, the vasa vasorum, develop new capillaries. Scar tissue finally heals the wound. Should the process be extensive, dilatation of the arch is certain to result, for the artery is being stretched eighty or more times a minute, and is thereby weakened. A sudden rise of blood-pressure at a very weak spot may produce a bulging. The extent of the pathological process in the aorta and blood-pressure determine the further development of the aneurysm. No clotting can occur in a fusiform aneurysm. Clotting and spontaneous healing may take place in a sacculated aneurysm. Dissecting aneurysms at times heal by clotting just as do sacculated aneurysms. The process is the same. There are no fibroblasts and hence there is no scar tissue. The clot becomes laminated and is usually of putty-like consistency when firmest.

Historical Summary.—Aneurysm has been known since the time of Galen, who, however, recognized only the traumatic variety. It was Vesalius (1543) who seems to have been the first to recognize and even to diagnose thoracic aneurysm. Ambroise Paré suggested the rôle of venereal disease. The relation between syphilis and aneurysm was demonstrated by Lancisi as long ago as the early eighteenth century. Nearly a century later Scarpa laid the foundation of the modern conception by demonstrating that the weakening of the middle layer of the artery was the important mechanical factor. The discovery of the *Spirochæta pallida* by Schaudinn in 1904 and the demonstration by Warthin and others of spirochetes in the wall of the aorta, proved the accuracy of the generalization of the relationship of syphilis to aneurysm which was pronounced two and a half centuries ago.

THROMBOSIS OF THE CORONARY ARTERIES

Definition.—A better name for this would be embolism of the coronary arteries, for it is the sudden blocking of a branch of one of the two main arteries or of one of the arteries themselves, which brings on the characteristic symptoms.

Etiology.—So far as is now known there is only one etiological factor and that is *age*. The great majority of the patients are over fifty years of age, although Herrick describes a case observed at autopsy in a man of forty-two, and the author saw at autopsy a case which had caused sudden death in a man of forty. However, such cases are unusual.

Again, it is a curious fact that *males* seem to be almost exclusively attacked.

Arteriosclerosis is present in the majority of cases. Some patients have enlarged hearts and hypertension; others have soft arteries and normal blood-pressure. Syphilis apparently plays no great rôle.

Some attacks have developed after a full meal, or following *exercise;* others have been precipitated by causes which are not discoverable. The patient may have had previous attacks of *angina pectoris.* Many cases have been observed among brain workers.

Symptomatology.—A man over fifty may suddenly be seized with agonizing pain over the heart and in the epigastrium. As in angina pectoris, the pain may radiate down the left arm; however, frequently, there is no radiation of the pain. Fear of impending death does not possess the patient. There is nausea, sometimes vomiting, cold skin, collapse, weak pulse and abdominal tympany. The lungs become emphysematous, moist râles are heard throughout the chest, the pulse becomes progressively more rapid and feeble, and the heart-sounds are faint. The heart dulness is diminished, due to the overlapping of the emphysematous lung. There is no fever. Death may occur within an hour, or the patient may live for several days. There is usually a clear sensorium up to within a short period before death. Although the pulse is feeble and the patient seems about to die, he may show unexpected strength, and be able to roll over in bed, or even to leave his bed and go to the toilet, as one of Herrick's patients did.

Occasionally the condition known as status anginosus develops, in which there is profound weakness; the slightest movement causes pain and the patient fears to move in bed as such activity produces a sensation of heart-failure. A certain amount of precordial distress, or even pain, is not uncommon, if the patient survives for several days. This is probably caused by the slight pericarditis which is found postmortem over the softened area of muscle. This pericardial friction has been heard during life in some cases.

Physical Findings.—If the patient is seen shortly after the attack, he presents an ashy countenance. The skin is clammy, the pulse feeble and rapid. Occasionally the rate is very slow. The blood-pressure is low, as a rule. There is irregularity of the pulse, with extra systoles or partial block. The heart-sounds are exceedingly faint. The arteries may be sclerosed. The heart is usually enlarged. The lungs are emphysematous and full of râles.

Diagnosis.—The most important diagnostic point has been shown by F. M. Smith in experiments on dogs; it consists in the inversion of the T-wave in the electrocardiogram. In dogs, after ligation of any branch of the left coronary artery, the T-wave immediately becomes more prominent, varying in height with the size of the artery ligated. Within twenty-four hours it becomes sharply negative in all leads, gradually becoming positive for the first time in Lead III. Herrick and Robinson have both diagnosed the disease in man by means of the electrocardiogram.

This disease must be differentiated from sudden accidents in the upper abdomen. The tympany, the referring of the pain to the epigastrium, nausea, vomiting, and collapse can easily be mistaken for perforating gastric or duodenal ulcer, acute hemorrhagic pancreatitis, perforation of the gall-bladder, hemorrhage into the adrenal capsule, etc. Furthermore, sudden pneumothorax or diaphragmatic hernia may be suspected. The absence of peritoneal irritation or inflammation, and the absence of fever and leukocytosis will aid in the differentiation. The presence of pain down the arm, a history of previous anginal attacks, arteriosclerosis, and enlarged heart, are points in favor of thrombosis. The fact that the heart is not dislocated, and that emphysema and râles are bilateral, should eliminate the suspicion of lung accidents.

Complications.—There is only one complication to be considered, namely, rupture of the heart; this usually occurs at or near the apex. Probably cardiac aneurysm is the result of occlusion of a branch of the coronary artery, from which the patient recovers. The myomalacia cordis following upon the anemic necrosis gives opportunity for aneurysm formation.

Clinical Varieties.—For convenience of description, and as a useful working basis, Herrick divides the cases into four groups:

(1) This group consists of cases of instantaneous death, in which there is no death struggle, the heart-beat and breathing stopping at once.

(2) To this group belong cases in which death results within a few minutes or a few hours after the obstruction occurs. These are the patients who are found dead, or who are clearly in the death agony, when the physician arrives after a hasty warning.

(3) This group includes cases of severity in which, however, death is delayed for several hours, days, or months, and in which recovery even occurs.

(4) This group is one which may only be assumed to exist, and embraces cases with mild symptoms, for example, a slight precordial pain, ordinarily not recognized, due to obstruction in the smallest branches of the arteries.

Treatment.—In a disease such as this there is little that can be done except to relieve the pain. This is best done by means of **morphin** injected hypodermically. Inhalations of **amyl nitrite** and hypodermic injections of **nitroglycerin** are **not** found to be efficacious. For a cardiac tonic, **digitalis** is found to be the best drug. Other measures depending upon the severity of the symptoms will naturally be used.

Prognosis.—The disease is usually fatal; however, this is not necessarily true. The author saw a case of a soldier forty years old who had dropped dead. Autopsy showed a complete, old, cord-like obstruction of the large descending branch of the right coronary artery. This must have been present for a long time. The soldier had been examined the day before death and had been accepted for general military service. There was no one extensive scar, but there was general myocardial fibrosis. The cause of death was a thrombus in a part of the large descending branch of the left artery, which had been narrowed by the early stage of endarteritis obliterans.

The severe cases all end in death. There may be cardiac collapse before death, which results in edema of the lungs and legs. Cheyne-Stokes respiration is not unusual.

Pathology.—It is now generally conceded that the arteries of the heart are not terminal arteries. There is more or less anastomosis among the terminal branches of the two coronary arteries. There seems to be individual variation, some men apparently having more anastomosis than others. This is certainly true of animals. The vessels of Thebesius, also, must be considered in the anastomosis. Consequently, a slow occlusion of even a large branch of one artery is not incompatible with good health and considerable bodily activity, as was illustrated in the above case which the author saw during life and at autopsy.

Experimentally, the ligation of a large branch of an artery is followed by acute softening of the part supplied by the occluded vessel. Upon the pericardial surface, this occasions inflammation, which results in fibrinous deposit and physical evidences of friction. Even if no arteriosclerosis is present in the arteries of the body, the coronary arteries generally reveal lesions of arteriosclerosis of the nodular type. The area of necrosis, following the obstruction of one of the large branches of a coronary artery, varies somewhat in extent, depending upon the number of anastomosing channels and upon the size of the artery. Externally, there is a more or less triangular depressed area, the base usually lying toward the apex of the heart. The area is pale in color and is soft, or firm, depending upon the age of the lesion. In the experimental animals, there is "often an area occupying the apex that is of soft consistency, regardless of the age of the lesion and of the amount of fibrosis in the surrounding tissue" (Smith). At the apex there is often extensive softening, in which the muscle is reduced to the thinness of paper. The degeneration is greatest on the endocardial surface. The papillary muscles also become softened and pinched off at the apices.

In dogs, the most constant lesions are those resulting from ligation of the ramus circumflex sinister. "The ligation of the first descending branch of this artery generally resulted in fibrosis of the anterior papillary muscle; the ligation of the posterior descending portion of the left circumflex artery resulted in fibrosis of the posterior papillary muscle" (Smith). Microscopically, the early lesions show pale staining of the muscle-fibers, and nuclei and infiltration with round-cells and red blood-cells. Later fibrous tissue cells are found, and the muscle-cells show advanced degeneration, until finally the whole area is replaced by scar tissue.

PERIARTERITIS NODOSA

Definition.—This is a rare and acute disease, which is characterized by pains in the muscles or joints, by fever, by leukocytosis, and by small aneurysmal dilatations on many of the smaller arteries, which lead almost invariably to a fatal outcome.

Etiology.—The cause of the disease is not absolutely determined. According to Lamb, there have been three main views:

(1) The syphilitic, which is now rejected by most authors. There have been no serological data to support it. Further, it is of interest that a similar disease is found in stags.

(2) The mechanical, which is only of historical interest. It was thought that high blood-pressure ruptured the media, which was later further injured by some toxic substance.

(3) The infectious or toxic view. This is the one now most commonly held. The organisms of the streptococcus group are thought to be responsible for the lesions. Some have thought that the *Streptococcus viridans,* specifically, is the one most often concerned. Others believe that any virulent streptococcus may cause the peculiar nodular lesions in the small arteries. The results of injections into animals have been uniformly negative, although Klotz claims to have produced perivascular lesions with *Streptococcus mitis* and *Streptococcus salivarius* in the arteries of rabbits. These lesions were inflammatory in type and had some slight resemblance to the lesions of human periarteritis nodosa.

Klotz collected 42 cases up to 1918. The youngest patient was two and one-half months, the oldest was fifty-seven years old. Males are affected more often than females, the proportion being 3 to 1. The condition seems to be most frequent in adolescence and early adult life. There are no predisposing causes.

Symptomatology.—There is nothing definite in the onset or cause of the disease which enables a diagnosis to be made with reasonable certainty. The onset may be acute or gradual. The development of symptoms is similar to that of almost any infection. There are pains in the muscles or in the joints. At times there is abdominal pain. Fever is usually present. There is weakness, prostration, and occasionally disturbance of sensation. In 61 per cent. of Klotz's cases there was edema of the ankles. The blood shows a leukocytosis of the polynuclear type. The urine may or may not contain albumin. The diagnostic criterion is the discovery of small nodules along the course of small arteries These were present in only 8 of Klotz's cases.

Diagnosis.—This is usually quite impossible unless there are the characteristic nodules on the arteries. There are no laboratory findings, and the data from blood-cultures would not establish the diagnosis of the specific malady. Final diagnosis is made only on the autopsy table, and even then it may not be accurately made on account of the small number of arterioles which may be affected. The microscopical picture establishes the diagnosis.

Treatment.—In a disease so difficult to diagnose, the treatment must of necessity be entirely symptomatic. Supporting measures are indicated. Water should be freely urged upon the patient. The diet should be light, with a preference for carbohydrates and fats. Fever is no contra-indication to food, provided the patient has an appetite.

Prognosis.—The prognosis is grave, if the diagnosis can be made during life. There is actually no opportunity for prognosis until diagnosis is made. Since this is practically impossible, prognosis must depend upon a careful valuation of all the symptoms, together with the course of the disease. The disease may last from one to several weeks.

Pathology.—The process is one essentially affecting the small arteries, more particularly those of the kidney, stomach, mesentery, liver and heart, and occasionally of the skin, thyroid, lungs, brain and spleen. The aorta and large branches show no involvement microscopically.

Klotz believes that the lesions of periarteritis nodosa differ from the common periarterial inflammations only in the peculiar manner of damage to the arterial wall. The distribution and the progress of the disease along particular branches of arteries is not unique for this lesion. Microscopical examination reveals a non-suppurative inflammatory process beginning in the adventitia. More acute inflammation reveals polymorphonuclear leukocytes, and later eosinophils are often found. The process extends along the lymphatics of the vasa vasorum to the outer coat of the media, where, at times, widespread degeneration occurs. The weakening of the wall produces small aneurysmal dilatations which frequently clot, and thrombosis of the vessel results The aneurysm is acute, that is, the clot is not laminated and cannot be differentiated from the inflammation in the vessel proper, inasmuch as the one merges into the other. The degeneration of the media is hyaline in character. It seems partly nutritional and partly toxic. In no case is the whole circumference of the vessel affected.

CLINICAL BLOOD-PRESSURE

Definition.—Blood-pressure may be defined as the force which is exerted by the heart-beat. It is measured, usually, in the brachial artery by means of an instrument which records in millimeters the force which raises a column of mercury above the zero point on a graduated scale.

Three figures in blood-pressure are recorded: (1) the maximal or systolic pressure, (2) the minimal or diastolic pressure, and (3) the difference between the two, the pulse-pressure. These constitute the blood-pressure picture and are usually written thus: 120—80—40 This means that 120 mm. Hg is the systolic pressure, 80 mm. Hg is the diastolic pressure, and 40 mm. Hg is the pulse-pressure. The three figures should in all cases be given. To this should be added the pulse-rate. The product of pulse-pressure times pulse-rate (P.P. x P.R.) equals volume output per unit of time. This formula, according to Erlanger, is correct for most cases, but it does not obtain under every condition.

Mean pressure is the average pressure at a given point, but it is not the arithmetical mean of the systolic and diastolic pressures. The mean pressure lies nearer to the diastolic pressure than to the systolic pressure.

Technic of Blood-pressure Measurements.—Various types of instruments have been used to measure the blood-pressure. Some are made with straight columns of mercury, some with a U-tube containing mercury, and some are made with a dial in which the expansion of thin plates of metal causes a hand to move around a central fixed point. The dial instruments are at present most frequently used. Much has been written about the relative merits of the mercury *versus* the dial instrument. At present it seems to be generally conceded that, for all purposes of blood-pressure estimation, the mercury instrument has no particular advantage in accuracy over the dial instrument. The dial is much more convenient. In fact, there is no absolute accuracy in any clinical blood-pressure instrument. The pressure in the brachial artery approximates, but does not equal, that in the left ventricle, and the pressure is subject to sudden fluctuations. The mistake has been made of paying too much attention to the blood-pressure reading alone. The public has become aware of the fact that life insurance companies refuse applicants with a blood-pressure above a certain point, and it has concluded that blood-pressure is a very important index to health. Importance, far out of proportion to their value, has thus been forced upon blood-pressure estimations. It is time that a saner view of the actual value of blood-pressure estimations should prevail.

The arm-band, which must be 12 cm. wide, is snugly, not tightly, wrapped around the upper arm so that the lower edge of the arm-band is from 2 to 3 cm. above the bend of the elbow. The patient should be sitting in a comfortable, relaxed position with the arm resting on a table; or he should be lying down with arm comfortably outstretched on the bed The air bulb is then rapidly compressed so that the pulse at the wrist is obliterated. By means of the escape valve, the air is gradually released so that the pressure in the arm-band falls. Systolic pressure is reached when the pressure above the compressed artery is just sufficient to force blood through it. It may be determined by palpating the radial and feeling the first pulse-wave, or preferably, by listening with the bell of the stethoscope over the artery at the bend of the elbow. The latter method, known as the auscultatory method, is the most accurate and the one most frequently used. As the pressure is reduced, five phases are differentiated as follows:

The first is a sharp, distinct click. This is the time to read systolic pressure. Then follows a murmur with the click or a murmur alone, the second phase. The third phase is ushered in by a loud snappy sound. This suddenly yields to a dull tone, the fourth phase. At this point, when the loud third tone suddenly becomes dull, the diastolic pressure is read This dull tone fades away into absence of sound, the fifth phase. In the normal person all these tones are readily heard.

In some cases of high blood-pressure the second phase murmur may suddenly cease, or it may be so feeble as to be scarcely heard. As the pressure is further reduced, the intensely loud third tone is followed by the fourth. Attention is called to this phenomenon, as neglect to bear this in mind may lead to error.

Certain ordinary precautions must be used in order to obtain reliable results. The cuff should be warm, and should be wrapped around the bare arm. When using the stethoscope, the bell should be placed firmly, but it should not press too hard on the arm. The artery must bisect the circle of the bell. Care must be exercised so that the edge of the bell is not tilted; this might compress the artery above or below the center of the bell. This faulty technic may produce tones which may occasion considerable error in the estimation.

It is generally agreed that the first sound, first phase, represents the systolic pressure. The author and others believe that the fourth phase is the point at which the diastolic pressure should be read. Some believe that the cessation of all sound is the diastolic point. Except in most high pressure cases, and in a few normal cases, the difference between these two points amounts only to 4 or 6 mm. Practically, it makes little difference which method is employed, provided one or the other is always used.

Mechanism of Maintenance of Blood-pressure.—The maintenance of the blood-pressure depends upon the pumping action of the left ventricle and the resistance offered to the flow of blood in the arterioles and capillaries throughout the body. This resistance is known as the peripheral resistance and is equal to the diastolic pressure. This force is exerted on the aortic side of the aortic valves during diastole and, therefore, represents the amount of dead weight lifted by the heart-muscle in order to open the aortic valves. The diastolic pressure always measures the force expended by the left ventricle to overcome the back-pressure exerted by the peripheral resistance. The actual driving-force which sends the blood to the periphery is the pulse-pressure. The large arteries act as distributing channels and the aorta especially acts as an elastic reservoir, which expands at each influx of blood during systole, and contracts on the column of blood during diastole. The driving-force during diastole is, therefore, the elastic rebound of the aorta. Changes in peripheral resistance are due to contractions of large areas of small arterioles or capillaries. Contraction of capillaries may be so extensive as to block off a large area and cause greatly increased peripheral resistance.

A further important factor is the venous flow. For the circulation to be in equilibrium, as much blood must enter the heart from the systemic veins during diastole as is discharged by the left ventricle during systole. In order that this may always occur, there must be an unobstructed venous return flow. Venous pressure must always be low. A rise of pressure on the venous side, due to engorgement, usually leads to a rise in diastolic pressure, and may lead at the same time to a fall of systolic pressure. The embarrassment of the circulation under such conditions is great, and the heart may not be able to respond with enough force to raise the systolic pressure.

Vasomotor System.—Although the driving-force is exerted by the heart, aided by the active elasticity of the great vessels, there would be no continuous circulation, unless there were some resistance against which the heart could pump. The control of the arterioles and probably of the capillaries, by the vasomotor system supplies the contractile tonus which makes possible the maintenance of the circulation. Probably the most important vasomotor area in the body is the splanchnic area. The arterioles and capillaries of this great area are capable of containing all the blood in the body, and in certain conditions, a loss of vasomotor tone in this area causes bleeding into one's own vessels.

Pressure on the abdomen may cause a definite rise in systolic pressure. The vasomotor system is composed of two sets of fibers, vasoconstrictor and vasodilator fibers.

The vasoconstrictor fibers have a bilateral center in the medulla which is always in a state of tone. Under certain conditions it undergoes rhythmical fluctuations known as Traube waves. "The axons leading from these medullary cells pass down the cord to terminate around cells of the anterior horn from the upper thoracic level to the upper lumbar, and constitute, with the medullary cell, the first neuron. The axons of the anterior horn cells are medullated and constitute the second neuron in the chain, the so-called preganglionic fibers. They pass from the cord in the white rami communicantes from the first thoracic to the second or fourth lumbar segments, and, entering the sympathetic chain, have one of three destinations. Those destined for the extremities end around cells in the sympathetic chain. The non-medullated fibers of these sympathetic cells constitute the third neuron, the postganglionic fibers. They pass by the gray rami communicantes back to the spinal cord and thence accompany the appropriate spinal nerves to their destination. The preganglionic fibers destined for the deeper vessels of the head pass through the white rami of the first to sixth thoracic segments and up the sympathetic to the superior cervical ganglion. From this point the associated postganglionic fibers are distributed through the carotid and other vascular plexus. The preganglionic fibers destined for the vessels of the abdominal and pelvic viscera pass directly through the sympathetic chain and by way of the splanchnic nerves to the celiac, inferior mesenteric, or other large prevertebral ganglia. From these ganglia the postganglionic fibers are distributed to the plexus around the abdominal vessels" (Norris). Pressor afferent fibers must end around the medullary center, bringing stimuli which lead to heightened tone and increased constriction of large areas. Also depressor fibers, which act to relax the tone, end around the center and cause dilatation of small or large areas.

Although there have been no vasoconstrictor fibers demonstrated in the vessels of the brain, there must be fibers which pass from the brain to the medullary vasomotor center. Mental work and mental strain produce an elevation of pressure by causing general systemic vasoconstriction.*

The vasodilator fibers are scattered throughout various nerves, for example, in the cervical sympathetic nerve, the chorda tympani, in the fifth cranial nerve, the splanchnic nerves, etc. From the first to the third sacral segments of the cord, dilator fibers pass to the hypogastric plexus and become the nervi erigentes, which are distributed to the corpora cavernosa of the penis and clitoris.

There is no single center for the vasodilator fibers. Probably there is a series of local centers which control the organs. The dilator centers are not in continual tone as is the constrictor center. It is not known how the fibers act on the muscular walls of the vessels.

EFFECTS OF CHEMICAL SUBSTANCES.—Various chemical substances have been found experimentally to influence blood-pressure. They may be inorganic salts, as barium chlorid; they may be alkaloids, as nicotin; or they may be substances derived from glands of internal secretion, such as adrenalin and pituitrin. In spite of the general impression that adrenalin is found in the blood and elevates pressure, a mass of data is now accumulating which proves that adrenalin is found in any demonstrable quantity only in the adrenal vein.

The injection of extract of the infundibular portion of the pituitary gland will raise the blood-pressure, but the effect is not prolonged. Various unknown substances resulting from vicarious metabolism must circulate in the blood stream and exert at times, or constantly, deleterious effects. If, as has been recently shown, the capillaries are contractile, such circulating substances could conceivably produce such widespread constriction as to lead to permanent changes in the blood-vessel and heart. Whether or not hypertension is produced in this manner is not actually demonstrated, but what evidence there is at hand leads to the belief that such a mechanism is a cause of the hypertension.

RESPIRATORY EFFECTS.—All are familiar with the record of blood-pressure taken with canula in the carotid artery of a dog. Here are seen rhythmical fluctuations of the record due to the respiration, a slight rise on inspiration, and a slight fall on expiration. Ordinarily these fluctuations, also found in human beings, during quiet inspiration, are so slight as to be a negligible factor in pressure estimations. In dyspnea or deep stertorous breathing the systolic pressure may be difficult to register. With the arm-band on and compressed, the point in the release of compression when the first tone is heard may vary at deep inspiration or forced expiration as much as 20 mm. Hg. Obviously both cannot be correct. The author's practice in such exceptional

---

* While no direct vasomotor control of the cerebral arteries has been actually demonstrated, analogy would lead us to believe that there is the same system of nerve-fibers, causing constriction and dilatation of the arteries of the brain, as is present in arteries of similar structure throughout the rest of the body. Some day they will be demonstrated.

cases is to take the average as the systolic pressure. Frequent subsequent estimations will reveal the average pressure.

It cannot be too strongly emphasized that one blood-pressure estimation has little or no significance unless it is made under rigid conditions and is absolutely within the limits of normal. Variations are so sudden that within a moment the pressure may show wide fluctuations. The respiratory mechanism assists in some of the fluctuations.

Average Normal Blood-pressure.—In healthy people there is an average normal blood-pressure which may vary considerably, but which tends always to assume the average for the age and sex of the person. Innumerable estimations have been made so that a good idea of what constitutes the average at decade periods can now be obtained. The following table is taken from a series of published figures of blood-pressure estimations:

TABLE 1. SYSTOLIC BLOOD-PRESSURE.

Age.	High.	Low.	Average.
15 to 30 years	142	104	123
30 to 40 "	145	107	126
40 to 50 "	147	110	128
50 to 60 "	150	117	133
60 to 70 "	156	121	138

The diastolic pressure is from 70 to 85 per cent. of the systolic pressure. Faught considers that 120 mm. is the average systolic pressure for a man twenty years old. For every additional two years of age 1 mm. is added. This is a fair working rule, but it places the systolic pressure for a man of sixty years at the upper limit of 140 mm., a figure which seems too low.

Kilgore (*Lancet*, Aug. 24, 1918) considers that the normal systolic pressure given in text-books is too high. Basing his figures on the examination of 500 students in the recumbent position, he found that quite a number were below 100, and an occasional one was as low as 85 or 90. He thinks that the systolic pressure should be retained as the most important measurement, and that palpation of the radial should be used instead of the auscultatory method.

It is seen that age has some effect on the blood-pressure, although this is not by any means always the case. Many persons eighty years of age have 120—80—40 for a pressure picture. The figures above indicate only that it could not be considered abnormal if a man of sixty should have a systolic pressure of 150 mm. Hg.

The diastolic pressure is normally below 100 mm. Hg. Usually it is from 70 to 90 mm.; in most healthy men and women it approximates 80 mm. The pulse-pressure is about 40 mm., but perfectly healthy persons are seen with a pulse-pressure of only 30 mm. Women, as a rule, have a systolic pressure slightly lower than that of men. The diastolic pressure in women is about the same as that in men.

With variations in the systolic pressures of normal persons amounting to 30 or more millimeters of mercury, it is of no particular importance to spend time estimating the systolic pressure by a series of half a dozen readings. The important point is to know that the pressure falls within the average for the age period.

The first reading is usually the highest, especially if the patient has never before had his blood-pressure measured. This should be discarded and the second reading taken. After some years' experience the writer has found that his average of three or four readings varies so slightly from any one reading after the second reading, that he has entirely discarded the method of taking the average of several readings. It is only in cases in which the person is excited and the pressure is at the upper limit that the average is sometimes taken. However, blood-pressure is not an absolute constant from day to day, or from hour to hour. A variation in systolic pressure of 20 mm. is not abnormal.

The diastolic pressure is quite constant. That is to say the variations at rest are rarely more than from 6 to 8 mm. As the diastolic pressure measures the peripheral resistance and the force which the left ventricle uses in order to start the blood in circulation, it is a better index to cardiac work than is the systolic pressure. The writer feels that too little attention has been paid to this part of the blood-pressure. Now, however, it is noticeable that all observers report the whole pressure-picture and most physicians concede the importance of the diastolic pressure.

VARIATIONS IN BLOOD-PRESSURE UNDER PHYSIOLOGICAL CONDITIONS.—That the blood-pressure of any individual is not a constant, unchanging force is well known. Many conditions affect the blood-pressure which cause marked fluctuations in the systolic pressure and which are perfectly compatible with normal hearts and normal vascular systems. Neglect to take into consideration the normal variability has led to error and to unnecessary mental anguish on the part of the patients. Some of the common variations are:

Diurnal.—Weyse and Lutz and others have shown that the blood-pressure varies somewhat during the day and tends to rise towards evening. The systolic pressure only is affected. The diastolic pressure remains practically constant.

Sleep.—During sleep the blood-pressure is the lowest for the twenty-four hours. As the early morning hours approach, the systolic pressure rises gradually. The pressure, when one wakes slowly and normally, is the lowest of any for the waking hours. The diastolic pressure is less affected than the systolic.

Posture.—There is a slight variation in the systolic pressure as one rises to a sitting or standing posture. It is highest in the standing position. On *a priori* grounds this would be expected. The difference is not great, usually not more than 10 mm. for the systolic pressure. The diastolic pressure usually rises slightly but not to the same degree.

Eating.—After a meal the systolic pressure always shows a slight, but appreciable rise. The pulse-rate is slightly increased and the volume output is greater. The diastolic pressure, as a rule, does not rise. Within limits the greater the meal, the higher is the pressure.

Exercise.—Exercise in the normal person always causes a rise in pressure. The whole pressure-picture rises, but the systolic rises faster and proportionately much higher than the diastolic pressure. A rise of from 30 to 40 mm. is not uncommon. The pulse-pressure is much increased. The volume output is greater, for the pulse-rate also rises and the product P.P. x P.R. is increased.

Emotional States.—The blood-pressure is greatly influenced by emotional states. Excitement, fear, apprehension of the physical examination, attention directed to the blood-pressure, concentrated attention watching the estimation, all tend to raise the systolic pressure. It is, therefore, necessary always to allay fear and to attempt to place the patient in as calm and relaxed a state as possible, particularly at the first examination.

Menstruation.—There is a slight premenstrual rise, but as a rule it is not great, and when the flow is established the pressure returns to its usual height. Women who suffer with great premenstrual pain are apt to have a greater rise in blood-pressure than those without pain.

PRESSURE IN THE DIFFERENT BRANCHES OF THE VASCULAR TREE.—At the heart the systolic pressure is greatest. As the branches come off from the aorta, the bed begins to widen until at the capillaries the arterial bed is at its widest and all pulse is lost. Only in states of great vasodilatation is the pulse transmitted as far as the capillaries. The most rapid fall in pressure occurs between the arterioles and the capillaries. The fall affects the systolic much more than the diastolic pressure, and finally the pulse-pressure is reduced practically to zero, the systolic pressure equaling the peripheral resistance. Any increase in venous pressure reacts at once upon the capillary bed and raises the capillary pressure more than it would be raised by an increased systolic arterial pressure.

Approximately, the pressure in the vascular tree at various levels is shown in the following schema:

TABLE 2. BLOOD-PRESSURE AT VARIOUS LEVELS.

	Systolic.	Diastolic.
Left ventricle	150	
Aorta	150	100
Brachial artery	120	80
Radial artery	100	70
Arterioles	80	60
Capillaries	20	20
Small veins	20	20
Femoral vein	20	
Inferior vena cava	3	

This schema lays no claim to accuracy, it shows only the general idea of decrease in pressure at the various levels.

In the recumbent position, the lateral pressure throughout the whole aorta is about the same. It has been shown, as would be expected, that the pressure in the femorals is greater than that in the brachials.

In the erect posture, the variations are greater because of the weight of the column of blood. The venous pressure is largely dependent upon the height of the column of blood above or below the level of the heart. Hence, for example, the pressure in the leg veins is greater than that in the arm veins. The veins are usually fuller in the lower extremities than in the upper.

Venous Pressure.—This has been a much neglected phase of blood-pressure. In the opinion of many men it is of more importance under certain conditions than is the arterial pressure. A simple and satisfactory, but rough, estimation of the venous pressure is secured by raising the hand above the level of the heart and by determining by measurement the distance above the heart at which the veins on the back of the hand are seen to collapse.

Eyster and Hooker have devised an instrument which can be used to measure the venous pressure in the superficial veins. The principle of the instrument rests on the use of the visible collapse of a vein on the back of the hand and the measurement of the forces necessary to collapse the vein in centimeters of water.

The instrument consists of a manometer which contains colored water and which is supported on a stand. This instrument is connected to a tube at the end of which is a small glass bell which is fixed over a vein by means of celloidin. A pressure bulb is attached at a Y on the tube. The patient's hand is placed on a level with the heart; the glass is fitted over a prominent vein by means of the celloidin, and pressure is exerted with the bulb. The point of the visible collapse of the vein seen through the glass is read in centimeters on the water manometer. Other more or less elaborate methods have been devised for recording the venous pressure, a full discussion of which will be found in Norris' "Blood-pressure and Its Clinical Applications." The venous pressure normally varies from 3 to 10 cm. of water. The greatest increase is seen in venous stasis, resulting from cardiac decompensation. Eyster maintains that increased venous pressure is the earliest sign of cardiac decompensation, and that it is the last condition to become normal when compensation is established.

Functional Tests in Relation to Blood-pressure.—When the heart responds to increased bodily activity, not only the pulse-rate but the blood-pressure rises. The rise is almost entirely limited to the systolic pressure, although the diastolic rises slightly, the pulse-pressure is increased, and blood-flow is faster. After exercise the pressure returns to normal; this should occur normally in a brief period of time.

Upon this series of facts, tests have been devised by a number of workers. Theoretically, some are correct, but practically all fall short of accuracy. The work required in executing some of the tests is so violent that there is clinical evidence of functional incapacity. Instruments are superfluous.

Were the arteries a system of rubber tubes with a known coëfficient of elasticity, it would be possible to measure accurately the functional capacity of the central pump. But when the vessels are under the control of the vasomotor system, are subject to various psychic influences, and vary in their size and elasticity, no method which has ever been devised is able to do more than approximate the functional capacity of the circulation.

Graüpner's test, in its original form, has been discarded. The principle was based upon the response to measured work with the legs recorded on a bicycle ergometer. By means of a brake the amount of work done can be measured. Cabot and others have modified this to either climbing a number of steps at a certain rate, or to walking up an inclined plane at a certain rate. The blood-pressure and pulse-rate are taken before exercise, immediately after exercise and every half minute, until the above rates return to pre-exercise figures. This has some value, but it is hardly as great as its enthusiastic advocates claim. In this test the blood-pressure rises in a normal heart, and the pulse-rate increases, but within three minutes it is back to the original figures. A poor response consists in a slow rise with rapid pulse and in a prolonged slow fall. A decline of pressure signifies a failing heart.

Another method described by Katzenstein was based upon the reaction of the heart to the compression of both iliac arteries. This, too has been discarded. More recently Barringer has used a measured amount of work performed with dumb-bells, or with a steel bar. The dumb-bells weigh from 3 to 20 pounds each. Calculation is based on foot pounds per minute. For example, two hundred foot pounds consist in lifting a five-pound dumb-bell above the head twenty times a minute. After exercise the pulse-rate and blood-pressure are taken every thirty seconds. The exercise is gradually increased up to the limit of mild fatigue by increasing the weight of the dumb-bells. Under normal conditions he notes a delayed rise in systolic pressure after heavy work. The appended chart shows the circulatory reactions in a normal man in increasing amount of work performed by means of dumb-bells. (The white perpendicular spaces represent the work periods in each experiment during which blood-pressure and pulse-rate could not be measured.)

Barringer considers that the delayed rise in systolic pressure is the essential feature. The time when it occurs and the amount of work performed measure the cardiac efficiency. He says, "Our *clinical experiments* demonstrate conclusively, we believe, that in the pulse-rate and blood-pressure reactions to graduated work we possess a valid test of the heart's functional capacity. If the systolic blood-pressure reaches its greatest height not immediately after work, but from 30 to 120 seconds later, or if the pressure immediately after work is lower than the original level, that work, whatever its amount, has overtaxed the heart's functional capacity, and may be taken as an accurate measure of the heart's efficiency." A study of Barringer's records leaves one unconvinced of the value of his modification of the work test. The author and others have failed to find much help in this method. Practically, the test, used by the Army Cardiovascular Boards in the recent mobilization, gives about as fair degree of information of functional capacity as the more elaborate tests. This test consisted in hopping on one foot 100 times. The blood-pressure and pulse-rate were taken in the recumbent posture. Immediately after exercise and every half minute thereafter, the pulse-rate and blood-pressure were taken. Within two minutes the pulse-rate should normally return to within four beats of its former rate, and the systolic pressure should also be back to its original height.

A much more accurate method of measuring functional capacity was employed in the examination of aviators for altitude flying. By means of a chamber in which the oxygen tension could be rapidly reduced to stimulate altitudes of thousands of feet, it was found that functional capacity could be very accurately measured. "In the case of well-compensated valvular disease, murmurs develop under low oxygen or become much stronger, and accentuation of heart-sounds takes place, indicating hypertrophy of the left ventricle or back pressure through the lungs; the blood-pressure is high and the heart is evidently overworking seriously. Often in young men such a heart will be fully as successful as a normal one in meeting the demands made on it in ordinary life; in fact, overcompensation is the rule rather than a failure to compensate. But under the low oxygen test the underlying defect is revealed.

"In the case of valvular lesions that are less well compensated, the heart is more readily reduced to incompetence; after the period of overwork there is marked cyanosis, excessive discomfort, and insufficiency of the peripheral circulation, most delicately shown by inability to perform well on the psychologic apparatus that forms part of the rebreathing test.

"In subjects with arterial disease, there is a more or less marked rise in blood-pressure, owing to inability of the peripheral vessels to make way for the increase of blood-flow without throwing a much increased strain on the heart. At the same time there is doubtless insufficiency of the coronary circulation as well, so that between high blood-pressure and poor nutrition, the heart muscle soon becomes incompetent; the heart sounds deteriorate rapidly in quality, and the peripheral circulation becomes insufficient" (Whitney, J. L.).

The energy index is a term applied by Barach to denote the total force per minute of the heart's action. He takes as the three well-established facts: systolic pressure, diastolic pressure, and pulse-rate. He multiplies the addition of the systolic and diastolic pressure by the pulse-rate per minute. This he terms the S. D. R. index, and contends that although it does not measure the work of the heart, it indicates the degree of activity of the circulatory system. Normally, the index is found to be about 20,000 mm. Hg pressure per minute. "A high index means increased cardiovascular effort; either the action of the heart and blood vessels is accelerated because of inability to accomplish their work at a normal rate of activity, or they are fully capable of doing their work, but the resistance to their functioning is great. Either condition is pathologic, and the variation of the index from the normal calls attention to this'' (Barach, J. H.).

As a matter of fact there is no method which is applicable to all cases. The problem is still open for solution.

Hypotension.—Constant low blood-pressure is a characteristic of certain individuals and seems in no way to limit their activities. Provided the pulse-pressure is over 30 mm. Hg, there is no essential reason why persons with systolic pressure of 100 mm. should have any symptoms. However, in many persons there is a train of indefinite symptoms such as headache, feeling of lassitude on slight exertion, mental depression, constipation, etc. Such people are usually of slight build, and have small bones and a long thorax with very acute costal angle. There is a tendency to splanchnoptosis, and general relaxation of musculature. The arteries seem small and are frequently palpable. The hands and feet are cold. The heart is long and narrow and the fluoroscopic shadow of the aorta is quite narrow.

Some of these people have what Sewall calls occult tuberculosis. There is no activity, but there are evidences of a slow fibrotic process which are shown most clearly by means of stereoscopic *x*-ray plates of the chest. The hilus shadows are large for the age of the person. The linear markings extend radially outward and upward almost to the chest-wall and into the apices. Scattered shadows, which are probably calcified, or fibrotic lymph-nodes, are discovered in the lungs.

Sewall has also called attention to the change in pulse-pressure which is produced by the assumption of either the recumbent or the standing position. The vasomotor tone is so low, especially in the splanchnic vessels, that the pulse-pressure falls when the standing position is taken. Either the systolic pressure falls or the diastolic pressure rises; however, the former usually occurs. The result is the same. The volume output of blood is lessened and the coronary arteries are not filled during diastole. Dizziness due to cerebral anemia is common and fainting is not infrequent.

The examination of the thousands of recruits for the army revealed a group of men who had breathlessness, palpitation of the heart, and precordial pain on slight exertion. Mental apathy, cold clammy cyanosed hands and feet, and frequently headaches, were also observed. Blood-pressure estimations on these men showed, as a rule, no hypotension; yet it might have been expected among such constitutional defectives. The subjects of true hypotension have little resistance to disease. They seem particularly prone to infection with tuberculosis; probably many are suffering from ''occult tuberculosis.''

The causes of essential hypotension are not known. Some have thought that it was due to cholin circulating in the blood, but this is disputed and has not been proved. Certain of the cases result from poor ancestry; in some there is syphilis in the antecedents. Graves contends that the scaphoid scapula is a frequent finding in hypotension. The assumption of a functional or constitutional defect in vasomotor control is begging the question, but it is the most which can be said relative to the cause of the condition.

Hypertension.—When the systolic pressure is constantly above the upper limits of the normal for the age and sex of the individual, it is designated as hypertension. Systolic pressure temporarily may be quite high, but it cannot be said to be hypertension unless it maintains a continued elevation. Prolonged hypertension is not a normal state. Sooner or later there are changes in the whole circulatory system.

Systolic blood-pressure may vary frequently and as much as 30 mm. Hg. Variations in the diastolic pressure are not so great. In fact, this pressure is quite constant. A rise which is continuous has as much, if not more, significance than a rise in systolic pressure. When the diastolic pressure is found to have a constant reading of 100 mm. or more, hypertension is present, whether the systolic pressure is 170 or 140 mm. In fact, if the diastolic pressure is 100 mm. and the systolic pressure 170 mm. the person may feel perfectly well. However, should the systolic pressure drop to 140 mm., while the diastolic remains 100 mm., there is insufficient pulse-pressure, and dizziness or fainting results. The drop in systolic pressure is usually the precursor of a failing heart.

Hypertension and chronic nephritis are not always necessarily associated. It is true that there are always microscopic evidences of kidney disease in every hypertension death. Functionally, many kidneys are normal according to all the usual tests. The criterion is not what the morphologist finds but what the kidneys are capable of doing during life. Kidneys which are functionally normal are for all purposes normal kidneys.

Occasional traces of albumin and hyalin casts in a urine of normal specific gravity do not always signify chronic nephritis. Such occasional findings in persons over fifty are not alone sufficient to diagnose nephritis in the face of normal function.

ETIOLOGY.—Various theories have been advanced to explain the condition, but none has been satisfactory. Many of the cases are accompanied by high diastolic pressure; others are found in which the diastolic pressure is below 100 mm. Hg.

Increased vasomotor tone throughout the body is one cause. But what produces the increased vasomotor tone? We know that certain drugs raise the blood-pressure temporarily. Injections of **adrenalin** and **pituitrin** (especially extract from the infundibular portion of the gland) also raise the blood-pressure. Voegtlein and Macht have isolated a crystalline substance from the blood of man and other mammals which they regard as a lipoid, closely related to cholesterin. This substance was recovered from the cortex of the adrenal gland. It increases blood-pressure. Whatever the substance is, it seems to be in the circulation and to exert its effect in one of two ways: (1) by stimulation of vasomotor center, or (2) by the direct action either upon the capillary area or upon the muscle-cells in the walls of the arterioles. In either case, peripheral resistance is increased. This raises the diastolic pressure and, consequently, the heart must pump harder to keep the blood in circulation. Hypertension is regarded by the author as a physiological response of the heart, directed toward maintaining the circulation in equilibrium under conditions which tend to produce vasoconstriction in large areas and to deprive these areas of blood. Hypertension is, then, a conservative process, but like many processes in the body, the conservative feature may in time become of real danger to the individual. Unless hypertension developed, in many cases the individuals would not live. There must be enough force to drive the blood through the body.

CLINICAL VARIETIES.—*Changes in the Heart Due to Hypertension.*—The circulation in its simplest analogy is like a pump and a number of distributing tubes which branch extensively. The velocity at the aorta is rapid; in the capillaries it is slow. A certain amount of blood, about 75 to 99 c.c. (Howell), is expelled at every normal systole. When the pump has to do more work, it acts as any other muscle does which is called upon for extra continuous work—it hypertrophies. The fibers of the heart become longer and larger, and consequently, the left ventricle becomes thicker and heavier. At the same time the cavity of the ventricle is increased in size. More blood is thrown out at every systole. The peripheral resistance forces up the diastolic pressure. The systolic pressure increases to such an extent that the pulse-pressure rises beyond the normal figure. At the same time that the heart is gradually becoming enlarged, the nutrition of the muscle suffers and connective tissue is gradually formed, thus actually paving the way for future weakness. The aortic valves become thicker, due to the extra strain put upon them.

Changes in the Arteries due to Hypertension.—Whether one believes that the heart first hypertrophies and produces changes in the arteries or that the arterial changes precede the cardiac, the changes in the arteries in hypertension are great. The distributing channels show a diffuse fibrous arteriosclerosis.

The vessels are often somewhat tortuous. In some cases they are firmer and smaller than normal; in other cases they are thicker and larger than normal. The fibrosis generally affects the media and replaces the elastic fibers so that the blood no longer flows through an elastic tube but through a more or less rigid one. Hence greater head of pressure must be maintained at the heart to force blood through these less elastic channels.

In the small arterioles, both intima and media are affected. The channels are narrowed by intimal proliferation, and the contractility and distensibility of the vessels are lessened by the loss of muscle-tissue. Therefore, a considerable force is necessary to drive the blood through the narrowed channels in order that it may reach the cells of the organs.

Probably the enormous capillary bed is narrowed in large areas and offers further resistance to the onflow of the blood.

Hypertension may be of serious moment to diabetics, inasmuch as it may raise the renal threshold for sugar excretion.

Hyperpiesis.—This is a term, meaning "excessive pressure," which Sir Clifford Allbutt proposed as a designation for those cases of hypertension which are not due to evident renal or cardiac disease. There is an arteriosclerosis which is the consequence of tensile strength, of excessive arterial blood-pressure persisting for some years.

HIGH PULSE-PRESSURE.—In every case of fully compensated hypertension there is increased pulse-pressure. Normally, the arch of the aorta, already filled with blood, and still contracting on the column of blood to force it onward, is suddenly and violently distended by the blood from the left ventricle. It is somewhat stretched, and as soon as diastole begins, it contracts upon the column of blood, held at one end by the closed aortic valves. Pulse-pressure measures the actual driving force which propels the blood to the periphery. If, then, the peripheral resistance is great, there must be a greater driving force at the pump. In all high pulse-pressure cases four conditions are found:

(1) Increase in the size of the cavity of the left ventricle. There is more than 90 c.c. of blood ejected at every systole.

(2) Increase in the width of the aortic shadow seen with the x-ray.

(3) Increase in the size of all distributing arteries, carotids, brachials, radials, femorals, renals, celiac axis, etc.

(4) The impairment of the percussion note over the manubrium sterni and bronchial to tubular breath sounds heard with the stethoscope.

Varieties of Hypertension.—All cases of hypertension are not due to the same cause or causes. There are several varieties. They may be roughly divided into the subacute and chronic hypertension cases.

Subacute Hypertension.—Under this heading come the hypertension of pregnancy and of eclampsia. In eclampsia the pressure picture is high, but after the uterus is emptied, the blood-pressure in many cases returns after a few weeks to its original level. Focal infections, exophthalmic goiter, and neurotic states may show hypertension until the cause is removed. Occasionally brain tumor, if complicated with asphyxia, and intracranial pressure from fracture of the skull, produce hypertension.

The hypertension found in many women at the menopause is at times not a chronic process. While these conditions are important, they are not as serious as are the chronic hypertension cases, which are divided into at least three groups.

Group 1.—Chronic Nephritis.—These are the cases with high pressure pictures, i.e., high systolic (200 +) and high diastolic (120-140 +) The pulse-pressure is much increased. The palpable arteries are hard and fibrous. There is puffiness of the lower eyelids; this condition is most pronounced in the morning on rising. Polyuria with low specific gravity, and nycturia are present. There are almost constant traces of albumen in the urine, with hyalin and finely granular casts. Functionally, these kidneys are much under normal. The functional capacity determined by Mosenthal's modification of the Schlayer-Hedinger method shows a marked inability to concentrate salts and nitrogen. The phthalein output is below normal. As the case advances, the phthalein output becomes less and less, until a period is reached when there are only traces, or when there is complete suppression at the end of a two-hour period. Such patients may live for ten weeks (as, for instance, in one of the author's cases), continually showing mild uremic symptoms, and then they may suddenly pass into coma and die.

The terminal condition in cases in this group is either uremia or cardiac decompensation (so-called cardiorenal disease). Cerebral accidents may happen to a small number. It is the author's opinion that the term cardiorenal diseases should be applied only to this group. However, the author once believed that all high systolic pressure cases should be diagnosed as chronic nephritis of some definite degree. From the purely pathological standpoint such a diagnosis is correct, but from the real, the functional standpoint, it is far from being the true condition of such cases. In this group, there is marked hypertrophy and moderate dilatation of the left ventricle, with dilatation and nodular sclerosis of the aorta. The kidneys are firm, red, small, coarsely granular, the cortex much reduced, and the capsule adherent. Cysts are common. It is the familiar primary contracted kidney. Mallory calls this capsular glomerulonephritis. The etiology is obscure. Often no cause can be found. Again, there is a history of some kidney involvement following one of the acute infectious diseases, or the nephritis of pregnancy. Usually, however, these cases fall into the group of secondary contracted kidneys—chronic parenchymatous nephritis.

Group 2.—Essential Hypertension.—One might designate this group as essential hypertension, or as the hereditary type, although there is not always such a history in an antecedent. This group includes the robust, florid, exuberantly healthy people. They often boast that they have never had a doctor in their lives. They are usually thickset or very large and fleshy. The pressure-picture is exceedingly high. The pulse-pressure is moderately increased. The arteries are rather large, fibrous, and often quite tortuous, although this is not always the case. Some of these individuals have small, hard, fibrous arteries. As a rule, there is no puffiness beneath the eyes, no polyuria, and no nycturia. The urine is of normal amount, color, and specific gravity. Albumen is rarely found and then only in traces; but careful search of a centrifuged specimen invariably reveals a few hyaline casts. The phthalein excretion is normal or only slightly reduced. The kidneys excrete salt and nitrogen normally. It is in this group that apoplexy is found most frequently. The rupture of the vessel occurs when the victim is in perfect health, often without any warning. Occasionally, when such a patient recovers sufficiently to be out of bed, cardiac decompensation develops later and he dies as a result of the cardiac complications. Pathologically, the hearts of such persons reveal the most enormous hypertrophy of the wall of the left ventricle. The cavity is somewhat enlarged, as is always the case when the pulse-pressure is increased, but the size of the cavity is not the striking feature. The aorta is fibrous, thick-walled, and the arch is slightly dilated. There are patches of arteriosclerosis. One patient, seen only at autopsy, had a rupture of the aorta just above the sinus of Valsalva; death had been due to hemopericardium. In such cases the kidneys are of normal size, dark red, and firm; the capsule strips readily, the surface is smooth or finely granular, and the cortex is not decreased. The pyramids are congested, and red streaks extend into the cortex. Microscopically, the capsule of the glomeruli are a trifle thickened; a few show hyaline changes. There is rather diffuse, mild, round-cell infiltration between the tubules. The tubular epithelium shows little or no demonstrable change. The arterioles are generally the seat of a moderate thickening of the intima and media, but it is not usual to find obliterating endarteritis. There is evidently a diffuse fibrous change which has not affected either the tubules or the glomeruli to any great extent.

When these patients with acute cardiac decompensation are seen, there is, of course, much albumin in the urine, and many casts, and the phthalein output is, for the time being, decreased.

Group 3.—Arteriosclerotic High Tension.—This might be called the arteriosclerotic high-tension group. Such patients are usually over fifty years of age. They are men and women who have led strenuous and dissipated lives, both physically and mentally. Often they have had periods of great mental strain. Many men in this group have been athletes during their young manhood. Many have been fairly heavy, although not excessive, drinkers. They are usually well-nourished and inclined to stoutness. The pressure-picture presents high systolic pressure with normal or only slightly increased diastolic pressure, usually below 100 mm. Hg, and high pulse-pressure. The arteries are large, full, fibrous, and usually tortuous. The heart is very large, the apex being far down and pointed outward. There is no polyuria; nycturia is uncommon, being, in fact, quite the exception. The urine is normal in color, amount, and specific gravity. Albumin is found only in rare instances, and hyaline casts are not invariably present. The phthalein excretion is quite normal, as is the excretion of salt and nitrogen. The terminal condition in most of the patients in this group is cardiac decompensation. They may have several attacks from which they recover, but each succeeding attack is produced by less exertion than the preceding one, and their control becomes more and more difficult. Eventually the patients become bed- or chair-ridden, and finally they die of acute dilatation of the heart. Occasionally patients in this group may have a cerebral attack, but in the author's experience this is uncommon. Pathologically, the heart is large, at times a true *cor bovinum,* and is dilated and hypertrophied. The cavity of the left ventricle is much dilated. The aorta is dilated and sclerosed.

The kidneys are increased in size, are firm, dark red in color, and have fatty streaks in the cortex. The capsule strips readily and the cortex is normal in thickness, or only slightly increased. The organ offers some resistance to the knife. The microscope shows small areas scattered throughout where the glomeruli are hyalinized, the stroma full of small round-cells, the tubules dilated, and the cells almost bare of protoplasm. Naturally the tubules are full of granular cast material. Also, the arterioles show extensive intimal thickening, fibrous in character, with occasional obliterating endarteritis. One has the impression that the small sclerotic lesions are the result of anemia and gradual replacement of scattered glomeruli by fibrous tissue. For the most part, the kidney, except for the chronic passive congestion, appears to be quite normal. One can readily understand that in such a kidney, function could not have been interfered with.

Hypertension Climacteric.—Many authors have called attention to the increase in blood-pressure in women at the menopause. Riesman gives the following points common to the group:

(1) The patients are usually stout, overweight and undersized.

(2) They have borne many children.

(3) They have neither a history nor any stigmata of syphilis.

(4) They are over forty-five years of age, the greater number being between fifty and sixty years.

(5) They are practically all constipated, and some of them suffer from intestinal indigestion.

(6) Up to a certain point, they show an amazing tolerance to pressures of high degree.

(7) In most cases the heart is enlarged, chiefly to the left.

(8) The arteries are soft, and even the retinal vessels rarely show any involvement.

(9) The kidneys, as far as it is possible to determine, are competent.

The symptoms which accompany such increased tension are thought by some to be due to the lack of inhibitory action of the ovarian secretion upon the thyroid, pituitary, and adrenal glands.

Cardiorenal Disease.—The author believes that this term should be reserved exclusively for those cases of chronic interstitial nephritis which develop decompensation as the result of the failure of the heart to maintain the hypertension necessary to life. In such cases the cardiac symptoms dominate the clinical picture. Under such circumstances the blood-pressure becomes a value in diagnosis. The estimation of blood-pressure in decompensation is difficult and only fairly accurate. However, the few very high systolic pressure tones which are heard over the brachial artery, below the blood-pressure cuff, reveal that the case is not one of pure cardiac origin. As the patient recovers compensation, the hypertension becomes definite.

Gull and Sutton, many years ago, gave the name arteriocapillary fibrosis to the cases of chronic nephritis. They conceived the idea that the pathological lesion was a general one, affecting not alone the kidneys, but the entire vascular system, the kidneys being affected simply in the course of the process.

The essential facts remain that in chronic interstitial nephritis there are widespread changes in all the arteries and in the heart, so that the heart is finally worn out by the attempt to force blood through the constricted vascular channels. Often the diastolic pressure is 180 or even 200 mm. In other words, in order to open the aortic valves the heart must perform an amount of work equal to or even greater than the normal heart performs at its maximum contraction. It is surprising for how long a time—years even—the heart is able to endure such a strain as is thereby placed upon it.

Meltzer called attention to what he termed "factors of safety" in the human organism. Here there is striking evidence of the factor of safety in the heart. In such a heart the reserve power is necessarily small. The organ is always approaching its maximum capacity and cannot suddenly take on a load without becoming dilated. This accounts for the sudden cardiac collapse in a nephritic patient, who has had no intimation that he was ill other than necessity of rising once or twice during the night to urinate. A bronchitis or a sudden physical strain destroys the delicate balance of the circulation and decompensation results.

Symptoms of Hypertension.—Hypertension is compatible with active and vigorous bodily and mental health. For an unknown period of years, perhaps, there has been a gradual increase in pressure. The increase is not without fluctuations. Diet, mental worry, and attacks of constipation have their acute effect, but there is a general tendency to a constant increase of pressure.

When symptoms occur, they may be confined to one system, for example, the cardiovascular, or renal, or nervous system, etc., or they may show complications in two or more systems.

The following groups may be recognized: (1) cardiac, (2) renal, (3) gastro-intestinal, (4) nervous, and (5) ocular.

Cardiac.—This group is characterized by dyspnea on slight exertion; cough; edema of the ankles, which may be worse at night and entirely absent in the morning; anginal attacks; precordial distress; feeling of effort in taking a long breath; and finally, great dyspnea, cough, bloody expectoration, anasarca, scanty high-colored urine, etc.

Renal.—This group is characterized by nocturnal polyuria of pale urine, cramps in the muscles, puffiness beneath the eyes, headache, and later by twitchings, convulsive seizures, sudden blindness, etc.

Gastro-intestinal.—Flatulence, distress after eating, and a tendency to constipation are marks of this group.

Nervous.—This group is distinguished by irritability of temper, nervousness, inability to concentrate the mind, flashes of temper, change of disposition, headaches, insomnia, and later by transient attacks of unconsciousness with temporary paralysis, larval apoplexies (Allbutt), and apoplexy.

Ocular.—Failing vision, retinal hemorrhages, and sudden amaurosis differentiate this group.

At the present time, when the sphygmomanometer is so widely employed, patients complaining of gastro-intestinal or of respiratory symptoms are not as frequently overlooked as they undoubtedly were in former days.

The combination of hypertrophied heart with the apex downward and to the left, ringing second sound at the aortic cartilage, signs of dilated aorta and high pressure-picture are readily found and indicate long-standing hypertension. It should be our aim to anticipate this advanced stage if possible. Early recognition does not rest altogether with the physician. Some men are fortunate enough to present themselves for life insurance examinations. Practically all companies now require a blood-pressure estimation, although some require only the systolic pressure. The fact that the applicant desires life insurance is usually evidence that he feels well and considers himself healthy. He works hard and plays hard. Others are not as fortunate in finding out that they have true hypertension while still free from all symptoms. They do not seek the advice of a physician until they notice one or more symptoms. They are often incredulous when told the true nature of their trouble.

There seems to be only one method of discovering the early cases of hypertension. People must be carefully examined at least once a year after they have reached the age of forty. The dentists now send cards to their patients reminding them that six months have elapsed since their teeth were last examined. It should be possible for physicians to urge yearly examinations upon their patients. Only in this way will we be able to curb the advancing hypertension before it reaches the point of permanent injury to the cardiovascular and renal systems. Until the physician is recognized as the guardian of health, as well as the restorer to health, there will be no decrease in the number of advanced cases of hypertension.

TREATMENT.—Since hypertension is considered to be a compensatory process, there is no more reason to treat it *per se* than to treat a case of compensated valvular lesion. A certain amount of hypertension is absolutely necessary to the individual's well-being. Were it possible to reduce the high pressure to normal, there would not be sufficient driving force to send the blood to the vital organs in the brain, and cerebral anemia would result. The high pressure is, however, a combination of the necessary hypertension and the hypertension due to some added factor. It is this latter element in hypertension which we should endeavor to eliminate. In hypertension which presents no symptoms and which is accidentally discovered, it is necessary only to regulate the **hygiene** and the **diet.** Most of these patients eat too much and take too little relaxation. It is the author's belief that meat of all kinds should be very much limited. People habitually eat too much. At rest the average man can keep in health on 2,000 calories daily. Certainly 2,500 calories should not be exceeded when the individual is moving about in normal activity It would be distinctly helpful if patients were fed on a caloric basis rather than by the usual haphazard method. The diet should consist of carbohydrates and fats, and large potations of water at meals should be prohibited. A heavy meal causes a distinct rise in pressure. **Rest** for half an hour after meals is helpful. Mild open-air **exercise** should be urged.

All evident **foci of infection** in teeth, tonsils, and accessory nasal sinuses should be thoroughly **eliminated.** Probably chronic infection in the gall-bladder and appendix should also be carefully investigated. **Hydrotherapy** is useful. Hot baths as well as very cold ones are to be avoided. An occasional **sweat-bath** under supervision is indicated. **Massage** is also to be recommended. A sojourn at a sanitarium where hydrotherapy and massage are systematically given is often of great benefit. **Electricity** has been used to reduce pressure. The high frequency current is the method most frequently employed. Autocondensation also has its ardent advocates. These methods are helpful, but the evidence that they actually reduce hypertension and keep it within reasonable limits is lacking.

Drugs are of no great value. The nitrites certainly do not help except temporarily; however, **erythrol tetranitrate** has the longest action in the body. Yet no one would seriously contend that this drug should be given except in selected cases. **Potassium iodid** in 1 gram (15.43 grains) doses twice or three times daily is often given, but the results are variable.

Macht has recently used **benzyl benzoate**, and has found it of value in some cases. An extended trial of this drug, in the author's experience, has not substantiated Macht's contention concerning its efficacy in cases of hypertension. Occasionally it seems to reduce the pressure-picture, but evidence that the reduction is due to the drug rather than to the enforced rest of the patients is not forthcoming. When the hypertension is due to toxic spasm of the arterioles, frequent **purgation** and administration of benzyl benzoate do lower the pressure-picture. However, it seems futile to give a drug which only temporarily reduces pressure and does nothing to remove the cause of the hypertension.

After all, the most efficacious treatment is a combination of hygiene, diet, and attention to the bowels, in conjunction with the removal of all foci of infection. When the various final accidents occur, they are to be treated as indicated in the sections dealing with uremia, decompensation, apoplexy, angina, etc.

PROGNOSIS.—As long as hypertension is devoid of symptoms, and is accidentally discovered in a routine examination, the prognosis is uncertain. In the midst of apparent health there may be apoplexy, decompensation, or uremia. An apoplexy is not necessarily fatal.

Pasteur lived for twenty-five years after a hemiplegia. A cardiac collapse is a serious matter and renders the prognosis grave. Patients rarely live a year after the first attack of cardiorenal disease. An attack of uremia is also a grave accident. As a rule, the patient dies within a year, although there are notable exceptions.

Occurrence in Various Conditions.—BLOOD-PRESSURE IN ACUTE INFECTIONS.—In all acute infections the blood-pressure either shows no change or is slightly lower than in health. At times, at the onset, the diastolic pressure may be lowered and the pulse-pressure slightly increased. As the disease progresses the pressure varies with the length of the illness. In a brief illness there is little change. In typhoid fever, for example, there is a considerable fall in the systolic pressure, and the diastolic also falls somewhat in the beginning of convalescence. The pulse-pressure is so low that any attempt to rise from the recumbent position brings on dizziness. In unfavorable cases the systolic pressure falls, the pulse-pressure is decreased and, as death approaches, the systolic rapidly falls to meet the diastolic, and circulation ceases.

In pneumonia Gibson first called attention to the ratio of pulse-rate and blood-pressure. When the arterial pressure expressed in millimeters of mercury does not fall below the pulse-rate per minute, the prognosis is still favorable. Should it fall appreciably below the pulse-rate, it has an unfavorable prognostic import. The rule is useful in many cases, but cannot apply to all. If the blood-pressure when the patient was healthy were known, it would be of far greater value. In all cases the sounds heard in the auscultatory phenomenon are of value. As long as the tones are sharp and clear, the heart is usually holding its own. When the third tone, especially, becomes soft and muffled, the first sound at the apex of the heart is usually impure and muffled, and the conclusion is justified that the heart is weakening.

BLOOD-PRESSURE IN CHRONIC INFECTIONS.—In the commonest chronic infection, tuberculosis of the lungs, the blood-pressure varies somewhat with the stage of the disease and the type of the individual. It has already been said that in the so-called occult tuberculosis there is hypotension. In the average incipient case in a previously healthy person, the pressure is within the normal limits. As the disease progresses there is definite hypotension and usually a decreased pulse-pressure. In gout there is apt to be hypertension, and in most gouty individuals there is also chronic nephritis, either of the interstitial or of the diffuse variety.

In chronic arthritis of the deforming type the pressure is usually low. In most of the chronic infections the tendency is toward low pressure, but there are many exceptions to this rule. Why a chronic focal infection, for example, should in one person apparently cause hypotension and in another cause hypertension is not altogether explainable.

BLOOD-PRESSURE IN SURGICAL CONDITIONS.—All anesthetics do not affect the blood-pressure in the same manner. An anesthetic is dangerous because of the narrow margin between a well-sustained pressure and a sudden drop in pressure. Among the common methods of anesthesia, the consensus of opinion now establishes the following in the order of their safety: nitrous-oxid-oxygen, ether, and chloroform. The latter is especially dangerous, because there is such a narrow margin between safety and sudden danger.

With any general anesthetic the pressure should remain constant during the anesthesia. Signs of danger are the falling of the systolic pressure and the increase in pulse-rate. The diastolic pressure may rise slightly, but the decrease in pulse-pressure is almost entirely due to the systolic fall. When the pulse-pressure reaches 20 mm. Hg, the patient is in danger. The indication given by the blood-pressure is more certain and occurs earlier than any other sign. No anesthesia should be given unless the blood-pressure cuff is on the arm and frequent readings at short intervals are taken.

Stethoscopes may be obtained with long tubing and a bell which is fixed to the arm over the brachial artery. The anesthetist can not only obtain the systolic and diastolic pressure quickly, but he can tell by the tones of the phases whether or not the heart is weakening. A well-given anesthetic with ether usually raises the blood-pressure at first. As the anesthesia deepens, the pressure becomes the same as during waking hours and remains there with slight fluctuations throughout the anesthesia. If the anesthesia is light, pulling on the parietal peritoneum causes a sharp rise. Rough treatment of the structures around the gall-bladder may bring on a slight fall. Even in deep anesthesia, pulling on the structures around the celiac axis where the solar plexus lies is evidenced by fluctuations on the blood-pressure. In the case of nitrous oxid-oxygen, if well given, there is less change than in that of ether. The initial blood-pressure rise is often absent. There is no struggling, but the patient falls into rapid unconsciousness. The chief danger here lies in a fall in the systolic pressure and a rise in the diastolic, due to the asphyxia.

With chloroform there is often a fall during the early stages of anesthesia. During full anesthesia a marked fall often occurs. This renders chloroform very dangerous. This fall usually ceases if the patient is managed properly, but it may suddenly drop further and death may rapidly supervene.

Lumbar Puncture.—In this operation there is usually a slight rise in pressure, which accompanies the skin puncture, and which increases when the dura is punctured. "Withdrawal of cerebrospinal fluid *per se* tends to lower the blood-pressure, but the net result of lumbar puncture is to raise it for at least twenty minutes afterward" (Gray and Parsons). A fall in blood-pressure is a signal for the immediate withdrawal of the puncture needle.

Shock.—In surgical shock the patient bleeds into his capillaries, which become engorged, and stasis results (Cannon). The blood-pressure falls rapidly. If hemorrhage is combined with shock, the fall may be greater, but shock alone, or hemorrhage alone, is capable of producing a fall so great that death results. McKesson's formula is that "a typical case of shock is characterized by a diastolic pressure of 80 mm. or less, a pulse-pressure of 20 mm. or less, and a pulse-rate of 120 or more per minute."

Blood-pressure in Obstetrics.—Normal pregnancy has no appreciable effect upon the blood-pressure. However, so important is the gradual rise of pressure in denoting toxemia that no one who practises obstetrics should fail to make frequent use of the sphygmomanometer. In order that a woman may be properly carried through a pregnancy, she should be seen within three months of conception. Then the blood-pressure should be taken. If the pressure is normal, it will be necessary to take it only once every two weeks or every month for the next four months. If at any time the pressure shows a rise, it should be taken daily until it falls—an indication that there was nothing wrong—or until it gradually rises, when the physician should begin to treat the patient for toxemia.

Hirst, Lynch, and many others have demonstrated the great importance of blood-pressure in pregnancy. While eclampsia is possible when the blood-pressure is normal, this is the exception. A rising blood-pressure is more indicative of the onset of eclampsia than all the urinary examinations. Both systolic and diastolic pressure rise. This is the most typical example of a toxemia producing widespread arterial constriction (or capillary constriction). It is an acute process which, if properly treated, disperses and leaves the woman in most cases apparently without complications. However, if kidney damage is present, there is no return to normal. During normal labor the systolic pressure rises on account of muscular exertion. After labor there is apt to be a general fall of the pressure-picture, due to exhaustion and to loss of blood. The pressure quickly returns to its normal figure, if the puerperium is uncomplicated.

Blood-pressure in Blood Diseases.—There are no particular changes in blood-pressure in diseases of the blood, except in anemias when the pressure is apt to be low. There are many exceptions to this statement. A falling blood-pressure is a bad omen and a falling pulse-pressure is a sign of heart failure.

Blood-pressure in Cardiac Diseases.—Blood pressure in cardiac diseases has been discussed under the various sections dealing with these diseases. Only one or two points will be emphasized here.

In aortic insufficiency the pulse-pressure is high, the diastolic is very low, even reaching 30 mm. Hg, and the fourth tone is frequently heard over the bare artery. A systolic pressure within the average normal range and a diastolic pressure of 50 mm. or below, is almost pathognomonic of aortic regurgitation.

In compensated true mitral insufficiency with enlarged left ventricle, the systolic pressure is usually in the upper zone of normal. In mitral stenosis the contrary condition is more apt to exist. The pressure falls in the lower zone of normal. In true aortic stenosis the systolic and diastolic pressures both show a rise. In decompensation the blood-pressure estimation often gives us information which auscultation over the heart or palpation of the radials fails to give. For example, the differences in the strength of individual beats are shown clearly, and the number of beats coming through at each mm. drop is distinctly heard. Any irregularities of rhythm are detected quickly when the cuff is on the arm.

A *pulsus alternans* is easily discovered by means of the auscultatory blood-pressure phenomenon. In this condition the beats are alternately large and small, and the rate is regular. This is of great value in prognosis, as well as in diagnosis, when digitalis is being administered in large doses. It is one of the results of mild digitalis poisoning. *Pulsus alternans* is also a sign of serious myocardial insufficiency. It is not always possible to detect it by palpating the pulse. The regular heart may give the impression that all is well, but the blood-pressure reading by the auscultatory method at once reveals the gravity of the patient's condition.

The Value of Blood-pressure Estimations.—No instrument, however precise, can serve for more than a part of a general examination. The sphygmomanometer is no exception to this rule. When used intelligently as a part of the physical examination, it has a distinct value and gives information which cannot be obtained in any other way. To expect the blood-pressure instrument to establish the diagnosis is absurd. So much propaganda has been disseminated by the sales agents of sphygmomanometers that physicians have been led to believe that it is an instrument which will make diagnosis easy. When the estimations are at variance with the statement in the little booklets accompanying these instruments, the instrument is apt to be blamed rather than the variations in human beings. The routine use of the instrument is undoubtedly of great value. The majority of estimations on patients will be found to fall within the normal limits, but that should not cause the instrument to be discarded, as it is not at fault.

In fevers, in cardiac disease, in pregnancy, in renal disease, in asthenic states, in anesthesia, and in many other conditions, the estimation of the blood-pressure at frequent intervals will be found to be most helpful in establishing a diagnosis and in assisting in the prognosis.

BIBLIOGRAPHY

Barach, J. H. Arch. Int. Med., Nov. 15, 1919, xxiv, 509.
Barrington, T. B., Jr. Arch. Int. Med., March, 1916, xvii, 365.
Herrick, J. B. Jour. Amer. Med. Assn., 1912, lix, 2015 (many references given).
——— *Ibid.*, 1919, lxxii, 387.
Pardee, H. E. B. Arch. Int. Med., 1920, xxvi, 244.
Sewall, H. Am. Jour. Med. Sc., Dec., 1919, clviii, 786.
Smith, F. M. Arch. Int. Med., 1918, xxii, 8.
Whitney, J. L. Studies in aviation. III. Cardiovascular observations. Jour. Am. Med. Assn., Oct. 26, 1918, lxxi, 1389.

CHAPTER II

ACUTE ENDOCARDITIS

By Henry G. Webster, M.D., F.A.C.P.

Definition, p. 67—Etiology, p. 68:—Exciting cause, p. 68—Pathology, p. 69.
Simple acute endocarditis, p. 71:—Etiology, p. 71:—Predisposing causes, p. 71—Symptomatology, p. 71:—Evanescent type, p. 71; Well-defined type, p. 72; Course of the disease, p. 73—Complications, p. 74—Treatment, p. 75—Prognosis, p. 77—Sociological aspect, p. 78.
Malignant endocarditis, p. 78:—Clinical varieties, p. 79:—Pyemic form, p. 79; Typhoid form, p. 80; Cardiac or recurrent form, p. 81; Afebrile form, p. 81; Cerebral form, p. 81; Chronic septic endocarditis, p. 81—Differential diagnosis, p. 84—Treatment, p. 85:—General management, p. 85; Hypodermatic treatment, p. 85:—Solutions, p. 85; Vaccine and serum therapy, p. 86—Prophylaxis, p. 86; Medicinal treatment, p. 86—Prognosis, p. 87—Occurrence and distribution, p. 87.
Identification of murmurs, p. 87:—Mitral regurgitation, p. 87; Mitral stenosis, p. 88; Aortic regurgitation, p. 88; Aortic stenosis, p. 88; Tricuspid regurgitation, p. 89—Bibliography, p. 89.

Definition.—Endocarditis—inflammation of the endothelium of the heart cavities, and particularly of the valves—is a general term which is often misapplied. While frequently employed to include the permanent valvular defects resulting from inflammation, the name should be limited to the more or less acute period during which the inflammatory changes are taking place, and "valvular disease," or some definitive term such as "mitral stenosis," used to indicate the persistent valvular defect and resulting circulatory and nutritional changes.

Endocarditis should be regarded as the local manifestation in the endocardium of a bacterial invasion originating in some such portal of entry as the tonsil, pharynx, teeth, uterus or other site of infection, and varying in its symptoms with the nature and virulence of the infecting organism. Under this conception of the disease it is possible to recognize and describe several manifestations, while their essential entity remains apparent. It is thus possible to group *simple, ulcerative, malignant, rheumatic, mycotic, septicemic, typhoidal, cerebral, embolic, chronic infectious* and other forms of endocarditis about a common center, and to reduce the varying terminology of several authors to comparative harmony.

As emphasized by Mackenzie, endocarditis is seldom a simple infection confined to the endocardium alone, but is usually accompanied by some degree of myocarditis, a factor to be remembered in explaining the precordial pain and oppression so often observed. In the more severe cases, at least, it would be better to use the term "carditis," indicating involvement of muscle, valves, endocardium, and pericardium.

Etiology.—EXCITING CAUSE.—The infectious agent in all instances is bacterial, varying in the degree of virulence. In the order of frequency these bacteria are the following: the *Micrococcus rheumaticus,* so-called, of Poynton and Paine, streptococci, notably the *Streptococcus viridans,* and, less frequently, the *Streptococcus hemolyticus, Staphylococcus pyogenes albus,* the pneumococcus, the *Bacillus influenzæ,* the gonococcus and the *Treponema pallidum.* In over 60 per cent. of all cases it is the *Micrococcus rheumaticus* that is isolated from the heart valves. Considerable doubt still exists as to the positive entity of the *Micrococcus rheumaticus.* This organism, variously called *Diplococcus* and *Micrococcus rheumaticus,* has been exhaustively studied by Poynton and Paine, whose names are frequently coupled with it, and it is regarded by them as the specific organism of rheumatic fever. It has been repeatedly isolated from the heart lesion, from the affected joints, and from other sources in the body. When obtained directly and transmitted to other animals, some doubt is thrown upon the specific character of the diplococcus, because it has been shown that it reverts to the ordinary streptococcus form when grown upon ordinary culture media; and that when injected it does not constantly cause both joint and cardiac lesions. (For a discussion of this subject the following authors may be consulted: Poynton and Paine, Triboulet, Westphal, etc., Meyer, Cole, Beattie, Longcope, Rosenow (*see* Bibliography).) The *Diplococcus rheumaticus* was responsible for 62.6 per cent. of the 150 cases of malignant endocarditis studied by Horder at St. Bartholomew's Hospital, London. In the vastly greater number of cases of simple rheumatic endocarditis we find about the same percentage, which varies from 80 per cent., reported by Cadet de Gassicourt, down to 36.7 per cent. from one of the German clinics. No positive percentage is as yet available for the pyogenic cocci. The *Streptococcus viridans* has been extensively studied by Libman, Rosenow and others. It has been isolated in eight of the writer's reported cases, and is doubtless more common than has been generally supposed. Hirschfelder lays emphasis upon the repeated presence of the gonococcus, which he insists should always be considered where cardiac disease complicates arthritis. Of the less frequently reported causes, the *Bacillus tuberculosis* and the meningococcus have been found postmortem. The *Bacillus influenzæ* of Pfeiffer is undoubtedly a potent factor, although its rôle is probably that of an adjuvant to other germs. Although myocardial complications are extremely common in grip, clinical endocarditis is by no means equally frequent, so that the influenza bacillus seems more prone to attack the myocardium than the valvular structures.

Of late years much stress has been laid upon the frequency with which a positive Wassermann is obtained in primary cases of aortic insufficiency. The reaction is obtained often enough to raise the question whether all cases of this particular lesion of primary occurrence are not definitely syphilitic. Characteristic changes in the aortic valves have been found by Longcope, and by Collins and Sachs, who found calcification of the valves with changes in the fibro-elastic layers similar to the usual syphilitic changes in the aorta. As one may occasionally observe clinically the advance of an aortitis coincident with aortic valvular disease, it is quite evident that the treponema plays a very important rôle in disease of this particular valve. Hirschfelder calls attention to a type of endocarditis, of which he gives an illustrative case, in which lesions precisely similar to those of syphilis may take place in the valves, especially at the aorta, but without the luetic organism. He quotes Ophüls to show the similarity of arterial changes, and claims an analogy between the two conditions. The writer has recently watched the development of an aortic regurgitant murmur in a boy of twelve, subsequent to an attack of polyarthritis, in whom a negative Wassermann was found, indicating that some cases, at least, are not syphilitic.

Various observers have reported endocardial complications in many of the acute infectious diseases, including pneumonia, small-pox, diphtheria and scarlet fever. The pneumococcus has been definitely identified by Wells in 4 per cent. of 517 autopsies where lobar pneumonia was the cause of death, thus substantiating the important rôle of the pneumococcus as a local infecting agent. Its toxic effect upon the myocardium has long been recognized as the most important feature of pneumonia. It has been reported that pneumococcus endocarditis may not appear for from 10 to 15 days after the disappearance of the original fever. It may therefore cause the suspicion of a late recurrence, or of an empyema. It seems likely that the ordinary pyogenic cocci have been the infecting agents of the other diseases mentioned, especially in scarlet fever, in which the involvement of the throat and tonsils is the probable source of secondary infection, just as the same germs may be derived from the pustules of small-pox.

Pathology.—The essential lesion in endocarditis is an inflammation of bacterial origin varying in degree and intensity with the nature of the infecting organism and the natural or acquired resistance of the patient between an ulcerative condition on the one hand and a hyperplastic one on the other. The heart-valves consist of a fibrous base covered on both sides with reflections of the endocardium, which projects in a double layer beyond the thinned out, fibrous base and forms the edge of the valve cusps, but a considerable portion of their surfaces are in contact, and, as was first shown by Virchow, it is along this line that the lesions first occur. It has been demonstrated (Wyssokowitch, Ribbert, E. C. Rosenow, Hirschfelder) that while toxemia predisposes to injury, it is the mechanical assault of the bacteria against the valves that initiates the lesion, and that valves that have become more vascular are more prone to such injury. With the roughening that results fibrin is deposited, mixed with lymph from the injured surface, and with bacteria. The resulting clot may organize in the less virulent cases or be softened and thrown off as emboli, or ulceration may more than keep pace with the thrombosis. The ferments peculiar to some of the more virulent types cause liquefaction, with destruction greater than the thrombosis. Ulceration results and may cause perforation, or the thinned out valve may rupture.

To recapitulate: In the *ulcerative type,* the lesion, due to the more virulent pyogenic organisms, begins as a roughening of the valve surface, which in some severe instances may involve the adjacent wall (mural type; mural mycosis). The fibrin deposits upon this roughened surface are liquefied, the base of the ulcer deepens. Necrosis extends, causing the detachment of the mixed mass of fibrin, bacteria and necrotic tissue in the form of emboli of varying size, but usually small. These are swept by the blood stream to distant parts of the body, where they may cause cerebral embolism, or lodge as septic foci, causing infarction of the lung, liver, kidney, or other organs.

In the *chronic type,* necrosis forms, but by reason of the patient's resistance, or because the infective agent is less virulent, a protective zone of leukocytes soon infiltrates the margins of the infected area, and in time a typical chronic inflammation replaces the acute process. New connective tissue strands penetrate the affected area, and gradually scar-tissue replaces the injured valve substance. The fibrin clots that have appeared on the necrotic surfaces are later penetrated by connective tissue growth, and, with the eventual development of blood-vessels, become fully organized. Endocardium slowly extends over the vegetation, and the healing is complete. Two conditions result, however. The deformed valve loses its power to coapt, and leakage is established; the increased vascularity renders it somewhat more susceptible to subsequent injury. If the new endothelial covering is for any reason delayed, or incomplete, re-infection is likely to take place, thus explaining the so-called recurrent form.

DYNAMIC FACTORS.—There are three factors which determine the changes of the heart action: First is the myocarditis, which, as Mackenzie points out, is practically always present to some degree. This is sometimes a simple granular degeneration, sometimes a more complete change with fatty infiltration or degeneration, and occasionally with more profound changes in the parenchyma of the muscle-cells, resulting in part from the presence of the bacteria, in part from the irritating bacteria with their toxins, and in part from the starvation due to the accompanying anemia. The second factor is the weakness incident to these nutritional and toxic factors, which results in a further lowering of tone, because of its effect upon the vasomotor mechanism. Lastly, the prolonged presence of the valvular defects produce a local and systemic changes which need not be discussed here, as they are dealt with in the section on chronic valvular disease. The combination of incompetent valves with weakened myocardium demands an increased exertion to compensate for the defects, and, as is the case with a child struggling with a burden beyond its strength, there is great waste of energy with further strain upon the myocardium, which tends toward ultimate dilatation. It is obvious that in order to supply sufficient blood for the peripheral circulation the ventricle must contract more forcefully and more often to compensate for the regurgitation, or to overcome the added resistance of a stenotic valve. Even in the acute cases the regurgitation into the auricles tends to set up edema, which in turn opens the way for a spreading infection and for irregular impulses with resultant arhythmia.

SIMPLE ACUTE ENDOCARDITIS

This form is by far the most common. It is the one almost invariably present in rheumatic infections, when it assumes one of two clinical varieties: a mild one, in which the cardiac involvement is only recognized after careful search, when it may give rise to a soft blowing murmur that sometimes disappears at the end of a few days, and a more severe one, in which the murmur becomes permanent. It may give no symptoms until later years.

Etiology.—PREDISPOSING CAUSES.—*Age.*—Rheumatic endocarditis is far more frequent in children, 90 per cent. of the cases occurring between the ages of five and fourteen years (Holt). Holt, Pisek, Lovett and others unite in calling attention to the fact that fully 90 per cent. of all cases in children accompany tonsillitis, chorea or rheumatism, whereas of older patients only about 60 per cent. are affected. It is also true in children that the cardiac manifestations are apt to be much more pronounced than the joint symptoms. Indeed, the constitutional symptoms may be nothing more than so-called growing pains, and the patient often not confined to bed, while the effect upon the heart may be very marked. Hirschfelder states his agreement with other writers that "rheumatic fever in children usually assumes the form of a tonsillitis with carditis and chorea, and is frequently devoid of any arthritic symptoms whatever." Recent observation of a considerable number of young adults has shown the writer that pharyngitis or tonsillitis, either alone or combined, is frequently the only precursor of a definite endocarditis.

As regards *sex,* the majority of authors state that men are more often affected than women. Statistics from the Methodist Episcopal Hospital show that three times as many men as women were affected, and grouped according to age, men under seventeen and women over thirty are less liable to the disease.

Symptomatology.—EVANESCENT TYPE.—The symptoms are primarily those of a simple valvular defect incident to the infectious disease that causes it. During an attack of rheumatic fever, chorea, tonsillitis, influenza, pneumonia, diphtheria, scarlet fever (occasionally), typhoid, and more rarely in some other acute febrile states, a murmur is discovered over one of the heart-valves. The patient shows no disturbance from this condition, and within a period varying from a few days to two weeks the murmur disappears. While many of these evanescent cases are explainable on the ground that they result from temporary changes in the valve openings, due to myocardial relaxation, some are doubtless caused by endocardial swelling that does not go on to roughening and fibrin deposits. No differential diagnosis can be made between the murmurs due to valve changes and those dependent upon the myocardial weakness caused by the fever and the accompanying anemia, but the condition must be kept in mind and its bearing upon the management of convalescence considered.

WELL-DEFINED TYPE.—As already stated, the early symptoms are those of the primary disease. As *acute rheumatic fever* is the most common, it may be used as a type. Shortly after the onset of the attack with its characteristic sore throat, fever, increased pulse, swollen, painful joints, sweating, furred tongue, scanty urine and progressive anemia, the patient may complain of precordial pain, substernal oppression, and dyspnea. Coincidentally the pulse-rate becomes more rapid, and slight irregularity is sometimes noted. The pain may be only a dull discomfort, or may be intense and stabbing. As both pleurisy and pericarditis are prone to develop in this condition, they must be excluded in determining the origin of the pain. Gibson declares that the more severe the rheumatism the greater the likelihood of endocardial infection. Mackenzie emphasizes the frequency with which slight arhythmias occur in rheumatic cardiac inflammation, and lays stress on this symptom as indicative of well-defined myocardial involvement. In this connection it must be remembered that pericarditis is seldom painful in itself, patients frequently presenting well-defined to-and-fro friction rubs that are discovered in the course of examination and have given no symptoms.

With the onset of precordial pain the patient may assume an anxious, distressed facies and require to be propped up to relieve the pain and dyspnea. The lips are apt to show a livid color, and the extremities to become a trifle dusky.

A *milder form* with a less distinctive clinical picture is often encountered about midway between the severe type and the mild evanescent form first described. Here the temperature is low, the patient but little depressed; in short, the constitutional symptoms are comparatively trifling, but there is malaise, a well-marked anemia, and a history of recent sore throat or possibly of recurrent attacks of tonsillitis, and the patient may still exhibit the swollen cervical glands suggesting infection of the tonsils. The tonsils themselves may be ragged and swollen, and seropurulent material is sometimes expressed from the crypts. There may be complaint of dull discomfort in the deeper muscles, which are often tender to pressure, though this is by no means constant. The pulse is a little rapid, but regular and of good quality, unless marked valve defects are present. The blood-pressure is usually within normal limits. If the condition has persisted for any length of time there may be edema. The combination of edema with low blood-pressure in such a case usually indicates a severe myocarditis and an infection probably more virulent than the symptoms would otherwise indicate.

Examination at this time is likely to show an increase in the area of the cardiac dulness and the presence of murmurs. At first only a trifling impurity in the sounds may be detected, but day by day the quality changes until well-defined murmurs are established. Of the various valvular sounds, two should be watched with particular care, the mitral and the aortic. The development of the mitral systolic murmur is readily followed by reason of its time and character, but the rapidity of the rate and predominance of the mitral regurgitant murmur not infrequently mask a mitral stenotic murmur that may be coincident and faint by comparison.

The development of an aortic diastolic murmur is at first appreciable as a faint shading off of the aortic closure sound, that steadily increases into a definite diastolic blow. With the increasing incompetence, the radial pulse shows the characteristic "water hammer" quality. Less often the tricuspid and pulmonary valves show involvement.

In estimating the probable origin of the valvular sounds, especially when considering the prognosis, three factors must be balanced—the actual valve lesion, the myocardial involvement, and the anemia. The anemia influences the myocardial tone, the myocarditis permits relaxation of the valve rings and produces relative incompetence, while the valvular insufficiency permits back pressure in the auricles and favors edema of the endocardium, which in turn tends toward additional injury. It is evident that the valvular murmur depending on the relaxed rings will tend to disappear with improved myocardial tone, and reduced edema will favor better coaptation.

COURSE OF THE DISEASE.—By far the greater number of cases of simple acute endocarditis go on to a symptomatic recovery. After a longer or a shorter period, largely dependent upon the character of the complicating disease and the nature of the infecting organism, the temperature falls, the systemic manifestations subside, and there are left only the anemia and the heart conditions. The myocardium tends to regenerate as the anemia is relieved. The germs either disappear, or else their presence ceases to produce symptoms. In many instances they doubtless become latent in the deeper structures of the affected valves. With rest and time, the reparative process produces organization of the vegetation with shrinkage, and endocardium grows in from the edges. The patient, in the average case, is left with one or more valves that are slightly incompetent, and a heart that has hypertrophied sufficiently to compensate for the leak, but, as has been indicated in the paragraph on Pathology, the increased vascularity, or the incomplete covering in by endothelium, or a combination of both, renders the affected valves peculiarly susceptible to subsequent attack.

The more remote effects depend upon the nature of the valvular involvement, and are fully discussed in the section on Chronic Valvulitis. But, by way of summary, it may be said that a slight mitral regurgitation with good compensation will not interfere with the ordinary activities of life, provided that the patient is not subjected to undue physical exertion, nor to unwholesome surroundings, and that he avoids dietetic follies. A slight aortic regurgitation may also be well borne for many years and, if the patient can be taught by graded exercises and the proper hygiene to bring both his cardiac and skeletal muscles into a state of healthful activity, he may fulfill the normal span of life. With mitral stenosis and aortic stenosis, and with tricuspid weakness, however, there is a definitely fatal outcome, which may be postponed, but not avoided. The ordinary changes incident to advancing age will inevitably exaggerate the existing effects, and all observers agree on the susceptibility to re-infection in any damaged heart. Therefore the patient must be warned not only against physical over-exertion, but also against exposure to disease. Influenza and the milder forms of epidemic infection are particularly dangerous, as well as the common forms of infection of the mouth and throat. The failure of the physician to insist upon the removal of infected tonsils in a patient who has had an attack of rheumatic fever, either with or without endocardial complications, cannot be too strongly condemned.

Complications.—Strictly speaking, endocarditis is itself a complication of other diseases, but it is usual to find pericarditis, pleurisy, renal, hepatic, pulmonary, cerebral and other infarctions mentioned as complications. The various manifestations incident to emboli lodging in other organs are discussed under Malignant Endocarditis, and need only passing mention here. Cerebral embolism is the most important, as it is the most frequent. Infarction of the lung may be extensive enough to cause a good deal of pain, and at times causes a considerable hemoptysis. Renal infarction may be evidenced by blood in the urine.

Pleurisy is a frequent and annoying complication of endocarditis. It not infrequently appears over the left lower lobe in the axillary region and spreads over the part adjacent to the pericardium, possibly by direct extension. During the dry, adhesive stage, and until fluid exudate separates the pleura, the pain is most distressing to the patient, and the limitation of motion and local inflammation tend to cramp and embarrass the heart. Sometimes a considerable serous exudate forms, and occasionally, after infection with the pneumococcus, empyema results.

Pericarditis manifests itself in either adherent, or serous, or, rarely, purulent pericardium. The adherent pericardium causes little distress and may only be discovered while listening for murmurs. A two-and-fro rub is its characteristic symptom. Effusion distends the pericardium and causes a decided increase in the area of dulness. Usually the heart sounds are distant and a little muffled. As has been said, pain is rarely present to any degree with either form.

Pleurisy and pericarditis are not infrequent complications. The pericarditis may be either of the type with effusion or of the adherent type. It is surprising how little disturbance pericarditis with effusion may make. Subjective symptoms are rare, and patients with adherent pericardium sometimes walk about with little or no discomfort. Its characteristic physical sign is a dry to-and-fro rub heard close to the ear and variously distributed over the precordium. It may be said to be more frequently heard over the apical region, and over the lower precordium near the sternum. *Pericarditis with effusion* may be extensive, and yet cause little or no cardiac embarrassment. It is fairly common as a complication of rheumatism. When present it may be recognized by the decided increase in the area of precordial dulness, which assumes a flask- or pear-shaped outline reaching as high as the second rib. A small spot of dulness at the base of the left lung behind is mentioned by Ewart as of diagnostic importance. As distinguished from pleurisy with effusion, *there is no pulsation to the right of the sternum.* Even with small effusions the heart sounds have a muffled, distant quality. Pleurisy is a frequent and often painful complication. It is by no means uncommon to find a small area of dry pleurisy over the lower axillary region, extending anteriorly to the pericardial edge that, except for the pain, may be taken for pericarditis. The pain persists until enough serum is thrown out to separate the painful surfaces.

A **snug bandage** or **adhesive plaster** strapping will usually relieve the pleurisy. **Opiates** may be required. The pericarditis usually requires no particular treatment.

Treatment of Acute Endocarditis.—The treatment of acute endocarditis must be directed against the two factors which make up the condition—the local lesion in the heart, and the general infection which caused it. If scarlet fever, typhoid, pneumonia or some other self-limiting disease originated the cardiac symptoms, the treatment is purely expectant, except in so far as reconstructive measures, including the relief of anemia, are indicated. If rheumatic fever precipitated the endocarditis, the field of treatment is somewhat widened. Arising as it does from the tonsils or peritonsillar tissues, including the pharynx, the site of the infection should receive thorough attention. Although there is some diversity of opinion among laryngologists as to the efficacy of local treatment, it is nevertheless perfectly proper to control absorption from the surfaces, as far as possible, and for this purpose **sprays** and **gargles,** as well as local applications, may properly be employed. **Hydrogen peroxid** cleanses by dissolving the necrotic tissue. Solutions of **sodium bicarbonate** (1 fluidram-1 pint [3.75 c.c.-473.0 c.c.]) tend to remove tenacious mucus and to restore the tone of the mucosa, while various organic silver salts, such as **argyrol** (15-20 per cent. solution), **applied locally,** are distinctly antiseptic. Crypts of the **tonsils** may conceal pus, and should be **explored** without too much violence. Strict **oral cleanliness** should be observed, especially as with rheumatic fever sordes are very prone to appear on the tongue and teeth. The **diet** should be light and nourishing. **Milk, gruels,** the lighter **cereals** and **fruit juices** may be included, and the total should be as nearly 3,000 calories as possible. **Lactose** may be advantageously added to bring up the total. Absolute **rest** is essential, not only to spare the sensitive joints, but to relieve as far as possible any additional strain upon the heart. It is surprising how few people realize the number of heart-beats per diem that can be economized by posture. For the same reason the **intestinal tract** should be kept as **free** as possible from gas, to avoid the irritating upward pressure of abdominal distention. Because of excessive sweating scrupulous care should be taken of the skin, and, to **avoid** the **chilling** of the **surface,** with consequent peripheral contraction and added cardiac burden, both bed-gown and bed-clothes should be of flannel or flannelette. The patients should be kept as cool as possible. Frequent **sponging** is also indicated, for the sake of cleanliness, and to relax the surface circulation. **Abundant fluids** are necessary to keep up the kidney excretion, and refrigerant and diuretic drinks, such as the cream of tartar lemonade, are efficacious for this purpose as well as grateful to the patient. While none of these measures have any direct influence upon the endocardium, they help to reduce the burden that the combined fever, local infection and general toxemia have thrown upon the heart.

Of the factors that act upon the heart itself, the rapidly advancing anemia is most important, next to the local infection, because the heart-muscle, already suffering from the degenerative influence of the general and local toxemia, is still further weakened by the impoverished blood supply. It is obvious that if the general tone of the heart-muscle can be sustained, dilatation with relative incompetence of the valve orifices may be avoided. Therefore some form of **iron** should be administered early, and a considerable choice is available. Basham's mixture (liquor ferri et ammonii acetatis 2 drams, or 7.5 c.c.) has the advantage of being a ferruginous tonic and a diuretic that does not irritate the stomach. The various **preparations of salicylic acid** enjoy a considerable reputation in the treatment of the arthritides. Many excellent clinicians doubt the efficiency of salicylic acid, and yet it has been so widely used and so generally depended upon as to merit the belief that it has some real value in rheumatic fever. The choice of a preparation and the size of the dose are largely matters for individual choice. In the writer's own experience acetylsalicylic acid, 5-10 grains (0.324-0.650 gram) every four hours, and strontium salicylate, 5-10 grains (0.324-0.650 gram) every four hours, seem to be less irritating to the digestive tract and therefore better borne, although many patients benefit by salicin and sodium salicylate made from the natural oil of wintergreen. Methyl salicylate, minims 5 (0.3 c.c.), with colchicin, 1/100 grain (0.00065 gram), in small repeated doses, seems at times to relieve pain promptly. If diuretics are necessary, dependence may be placed upon the **theobromin compounds** such as diuretin, 10 grains (0.65 gram), and theocin, 10 grains (0.65 gram), while **potassium bitartrate, potassium acetate** and **potassium citrate,** 10-30 grains (0.65-1.95 grams), alone and in combination, are dependable.

Digitalis is discussed in a paragraph on the treatment of malignant endocarditis, but for the sake of emphasis it may be well to repeat here the statement that small doses of digitalis, minims 5 (0.3 c.c.), of any reliable preparation, given early, are helpful in the early stages before evidences of decompensation appear. It must be remembered that digitalis reaches its full effect upon the heart-muscle slowly, and that therefore valuable time can be saved by beginning digitalis medication early; the small doses are not sufficient to disturb a myocardium that is functionating properly. Of other cardiac stimulants, **strophanthus (tincture),** minims 4 (0.24 c.c.), **caffein citrate,** grains 1-2 (0.065-0.130 gram), **spartein sulphate,** 1 grain (0.065 gram), are each of value. **Camphor,** grains 3 (0.195 gram), in oil hypodermatically, can be depended upon for temporary help. It should be repeated at short intervals from one to two hours. **Strychnin sulphate,** grain 1/60-1/30 (0.001-0.002 gram), is occasionally helpful. However, while it is a general muscular stimulant, it also acts upon the central nervous system and may produce undue mental excitement. Many clinicians recommend the intravenous use of **strophanthin**, grain 1/100 (0.00065 gram), hypodermically, to meet the emergent conditions incident to acute dilatation.

The precordial pain that is not infrequently a distressing symptom is at times relieved by an **icebag**, and at other times by a **sinapism**, but not infrequently demands **morphin**. A single small dose of 1/6 or 1/8 grain (0.10 or 0.008 gram) hypodermically not only relieves the pain, but tends to slow and steady the heart action.

Prognosis of Simple Acute Endocarditis.—As Mackenzie points out, the question of prognosis is the one vital matter in all cases of heart disease, a point that is too often overlooked or forgotten by the average practitioner. It has become a matter of routine to consider the mechanical defects of a damaged heart without balancing against them its remaining capacity. For this reason it is not merely enough to identify the nature and extent of a valvular defect, nor the combination of more than one murmur. In giving any estimate of the seriousness of cardiac disease, it must never be forgotten that the average person attaches tremendous importance to heart disease, and that the very name carries with it a subconscious terror. Curiously enough the laity are prepared to accept with more or less courage and hopefulness a diagnosis of muscular weakness, but are terrified when told they have a leaking valve. Extended experience with cardiovascular cases, especially during the recent examinations for the draft, has served to show how important it is that the patient's mental conception should be taken into consideration in making any diagnosis. Furthermore, the conviction has been strengthened, as a result of the same observation, that altogether too much importance is attached to mere valvular defects, and that for the ordinary occupations a very considerable valvulitis is compatible with useful activity over prolonged periods. It is therefore necessary to give an extremely guarded prognosis of any case of acute endocarditis, and to reserve final judgment until the patient has so far recovered that the capacity of the heart to respond to various tests, and varying degrees of stress, may be determined. In making such a determination a great deal of weight should be attached to the patient's own subjective sensations. A sense of substernal oppression or of constriction about the upper chest, dyspnea, precordial pain, are guides indicating the extent of the capacity of the heart-muscle and the great vessels to perform their work without strain. One should note whether the quality of the heart sounds improves under moderate exercise, and how rapidly the pulse-rate returns to normal after acceleration by exercise. The variations in rate caused by pressure upon the vagus nerve with the finger, during auscultation, should also be most carefully noted. It is a wise measure to test the heart after brief active exercise and at the end of a day of continued moderate stress. Many patients with considerable involvement of the myocardium, as well as of the valves, are able to indulge in active intermittent exercise, yet they cannot stand prolonged moderate exercise: they can play tennis for a time, but cannot walk up moderate grades. By far the greater number of cases of acute rheumatic fever recover completely with very moderate permanent valvular defects; in many instances murmurs which were loud during the height of the fever disappear completely after the fever and anemia have subsided and the myocardium has recovered its tone. Again, many such murmurs will practically disappear in the resting heart, but may be brought out after active exercise. And yet again, some hearts that show a slight murmur and some irregularity will become steady to a remarkable degree under exercise. If the mitral valves alone are affected, and such murmurs are found to be accompanied by little or no hypertrophy, the outlook for the patient is good. Even when a slight degree of aortic regurgitation is combined with a mitral insufficiency—provided there is a reasonable compensatory hypertrophy—the outlook for a long and useful life is good. If mitral stenosis exists the outcome is eventually assured, and yet many sufferers from mitral stenosis get on very comfortably until after the degenerative changes of middle life begin. This statement is also true for aortic stenosis. A factor of uncertainty in every case of endocarditis is the inability to foresee whether or not recurrent attacks are likely.

Sociological Aspect.—The bearing of acute endocardial affection upon *marriage* and *childbearing* is comparatively negligible, except that during an acute attack the question may be raised of the future bearing of the disease on a marriage that has already been planned. As has been already emphasized in the paragraph on prognosis, one should not commit himself as to the future until sufficient time has elapsed to determine the reserve force of the patient. The mere presence of a murmur should not condemn the patient to an unmarried life, for many cases of mitral regurgitation live in comfort and usefulness for many years. Were we to condemn every young man in whom a murmur can be demonstrated to celibacy, it would be a serious injustice. In general, it may be said that the presence of mitral stenosis or aortic stenosis requires careful counsel and a thorough explanation of the probable outcome in every instance, but that well compensated mitral regurgitation should not be regarded as incompatible with a long and useful life and the assumption of family cares. The bearing of mitral stenosis on pregnancy and parturition cannot be discussed here, but most accoucheurs regard the combination with foreboding, and many excellent men strongly favor the early termination of such pregnancies.

MALIGNANT ENDOCARDITIS

As has already been emphasized, malignant endocarditis is in reality a general infection with involvement of the heart-valves. As in the other forms of endocarditis already described, its manifestations are twofold: those referable to the general septicemia and those dependent upon the valvular involvement. The disease is protean in its manifestations

It may simulate typhoid fever, or acute pyemia, or it may be afebrile, or it may occur as a recurrent febrile exacerbation of a preëxistent valvular disease. Osler includes, as well, a type to which he gives the name of *chronic septic endocarditis,* which differs essentially from the other types in its more protracted course. As Osler's terminology has been generally accepted, his classification will be followed here.

Clinical Varieties.—(1) THE PYEMIC FORM.—*Symptomatology.*—As the name implies, this type is generally ushered in by the usual evidences of an acute purulent infection coming on postpartum, or following intrauterine manipulation, or subsequent to an infected wound, or to tonsillitis or abscess formation anywhere. Not infrequently, without a history of previous infection, severe constitutional symptoms will appear, such as chills, commonly repeated, fever, prostration, possibly vomiting, not infrequently profuse sweating, and sometimes delirium. There may be hematuria; anemia appears early and is rapidly progressive, with a well-marked icteroid color to the skin, which is dry, except during the chills. Thrombophlebitis sometimes develops, from which septic emboli may give rise to hemiplegia or infarction of the lung and kidney. Sometimes the fundus oculi is affected by thrombi or by hemorrhage, varying from slight spots to general retinitis and blindness. At times the spleen becomes affected, with engorgement and pain in the back. Septic infarction of the lung may cause bronchitis or bronchopneumonia. Involvement of the heart-valves may manifest itself early and develop rapidly, or it may not appear for several days, and occasionally may be so much delayed and so indistinct as to leave the diagnosis in doubt, as far as the heart is concerned.

The heart and pulse bear the chief brunt of the disturbance. The heart-beat is rapid and rather feeble, and the blood-pressure correspondingly low. The systolic pressure varies from 105 to 90, the diastolic from 80 to 50. It has been remarked that, while a dicrotic pulse is frequently observed in early typhoid, the pressure is too low and the rate too rapid for it to occur here. Although the mitral and aortic valves are the ones usually affected, the virulence of the disease may cause such rapid progress that the first evidences of valvular involvement are found over the tricuspid area, due to the progressive myocarditis and the engorgement of the systemic circulation. Any one or all of the valves may be affected, and it is common to find jugular pulsation and, not infrequently, pericarditis. The manifestations are so various that no detailed description of each individual valve need be given. The characteristic physical signs of the individual valves will be found tabulated on page 87.

As circulatory failure progresses, the liver may become engorged and extend appreciably below the costal margin, and pulsation may be present; septic infection of the liver may ensue, and jaundice become deep enough to suggest acute yellow atrophy. In passing, it is well to remember that transmitted impulses from the deep abdominal vessels and from the heart may simulate liver pulsation.

Embolism of the kidney has already been mentioned. It is frequent enough to be constantly borne in mind, and may be either a single infarction or the multiple miliary abscess formation which is apt to follow infection by the pyogenic streptococci. Infection of the kidney is usually heralded by a sharp chill, and there is not infrequently deep lumbar pain and vomiting. The urinary findings vary with the degree of infection, and there may be casts of all descriptions made up of both red and white blood-cells, besides the common granular and hyalin types. Albumin, of course, is apt to be present as in any febrile disease. The urine is generally concentrated, scanty, and of high specific gravity, and may contain free blood or hemoglobin. Not infrequently bacteria can be demonstrated.

The particular type of infecting organism determines a wide variety of phenomena, such as affections of the joints, skin and other tissues, as in any true pyemia. Thus one may find eruptions varying from the small purpuric type to the widespread hemorrhagic or ecchymotic, the nodular and the furuncular sorts. Periostitis has been found, arthritis of a wide variety of joints, and hemorrhages from mucous surfaces, including the nose, the pharynx and the alimentary tract. The peritoneum is sometimes involved, and ascites and edema are not uncommon.

The *diagnosis* rests upon the blood culture, where the infecting organism may be demonstrated in over 90 per cent. of the cases. Failure to find the germs is much less common in the septicemic type, which is due to the more virulent cocci. As one would expect, blood destruction is the rule, resulting in a low red-cell-count with diminished hemoglobin and a high polymorphonuclear leukocytosis. The temperature range is too variable to be diagnostic. It is usual to find extreme variation during the day, and sometimes the antemortem rise is replaced by a steady fall of temperature, which may incite false hope of recovery. But the temperature range is often abnormally low from beginning to end.

The mental symptoms range from active delirium to lethargy and coma, and in those occasional cases where the meninges are involved the characteristic symptoms of meningeal irritation are present.

The *course* varies from a few days to three or four weeks. The *outcome* is almost always *fatal.*

(2) THE TYPHOID FORM.—As the name implies, the *symptoms* are those suggestive of typhoid fever. Without ascertainable history that points to any of the ordinary modes of infection, the patient develops a slowly increasing fever with a dry typhoid tongue, more or less mental hebetude, or delirium, and chills or chilly sensations. The spleen may be enlarged. Occasionally petechiæ are present.. There may be a little bronchitis. Nausea has been observed, and there may be diarrhea. As in the previous type, cardiac symptoms are variable—at times the presence of herpes labialis or of petechiæ, combined with the irregular fever and the mental symptoms, may strongly suggest meningitis. The resemblance to both meningitis and acute general miliary tuberculosis may be striking, and only a positive blood culture will clear the diagnosis. A polymorphonuclear leukocytosis is the rule and this should

help to differentiate it in the absence of a Widal. The *course* of the symptoms may vary from three weeks to as many months, with occasional remissions.

(3) CARDIAC OR RECURRENT FORM.—This form presents a somewhat different picture. In this type there is already existent a well-defined valvular disease, during the course of which the patient develops a febrile attack with evident extension of the endocardial involvement. In the milder cases this condition subsides only to recur after a few days or a few weeks. Some patients will show recurrences for several years. The following case history, given in brief, illustrates a well-marked case:

M. G. Female. Twenty-two years old. Single. Housemaid. Entered the Methodist Hospital with dyspnea, cyanosis of the lips and fingers, anxious expression, precordial pain with some bulging, marked venous pulsations in the neck, rapid and irregular pulse, low blood-pressure, moderate edema of feet and ankles. There was a history of acute rheumatic fever four years previous. She had a low irregular temperature varying from 99.5° to 101° F. (37.4° to 38.3° C.) for about ten days. When admitted there was moderate cardiac hypertrophy, the left border of the heart extending 11 cm. from the midsternum, and there were both mitral stenosis and regurgitation. After rest and treatment she was able to leave the hospital in about two months, and three weeks later was readmitted with a recurrence of all symptoms. During this second recurrence the aortic valves became involved, but she nevertheless made a symptomatic recovery, and was able to leave the hospital in two months, only to return in a few weeks with a third, more severe, and eventually fatal recurrence.

Cases of this type, however, may show much shorter afebrile periods, the remissions lasting only a day or two at the most and progressing to a *fatal issue* after a few weeks.

(4) AFEBRILE FORM.—This form is of much less frequent occurrence. It is characterized by pronounced toxemia, *cardiac symptoms* and a more *protracted course.*

(5) CEREBRAL FORM.—Some writers still further subdivide and classify under this name those cases of primary endocarditis in which cerebral embolism is, if not the first, at least a very early symptom. There may be a day or so of malaise, fever, chills and then a sudden hemiplegia. The cerebral symptoms vary with the size and position of the embolus. Death may ensue in a few hours without a return of consciousness, or it may be more remote, and result from septic meningitis or from encephalitis. Aphasia is common in the less severe cases. The question of prognosis depends upon the ability to differentiate between this septic form and the occurrence of the more common types. As some degree of valvular vegetation is present in almost all cases of both types, the diagnosis must rest upon the blood culture. If the characteristic petechial eruption of malignant endocarditis is present, it is suggestive.

(6) CHRONIC SEPTIC ENDOCARDITIS.—Chronic septic endocarditis is the name given by Osler to a type of case that runs a prolonged course

varying from three to fourteen months. Since the appearance of his original monograph considerable study has been given to this type of case, and much has been added, especially by the careful studies of Libman and Celler, while the bacteriology has been amplified through the observations of Rosenow and others. While these cases often present such a variety of symptoms as to make them extremely difficult of determination, at least in the beginning, they later assume characteristics which serve to identify them. Three *symptoms* are declared to be pathognomonic: tenderness over the lower end of the sternum, a petechial eruption, and erythematous nodules. A prolonged irregular temperature is characteristic. Cases of the sort may often begin with a tonsillitis; authors have called attention to a yellowish exudate which fills the crypts of the tonsils and is supposed to be suggestive of the type in question, but unquestioned cases are on record in which the primary focus of infection was a pharyngitis without exudate. Shortly after the appearance of the tonsillitis, a murmur is made out over one or the other group of valves, and a persistent, though somewhat irregular, temperature of the septic type is established. There may be a little puffiness about the ankles, and the pallor of the skin, with a low blood-pressure and somewhat rapid pulse, calls attention to the fact that there is infection of more than usual virulence. A blood culture will often demonstrate the presence of the *Streptococcus viridans.* This type, however, may vary and may present merely the temperature and cardiac symptoms with gradual involvement of the kidney, possibly enlargement of the spleen or liver, or both. There are progressive emaciation, nausea and vomiting, and occasional crops of either a petechial eruption, most often seen about the ankles or calves, or an erythema nodosum. Some clinical observers insist that the petechial eruption is characteristic of *Streptococcus viridans* infection, and that the painful nodular type is more apt to be found with either the *Staphylococcus pyogenes albus* or with one of the hemolytic types. In the writer's personal experience both types of eruption have occurred in cases in which the viridans has appeared in the blood cultures. There are also cases of the sort which are clinically identical, but in which no growth can be obtained, a condition that is explained by the occurrence of the germs intermittently in the blood stream. It is worth noting that in some of the less severe types the only symptoms may be a mild evening rise of temperature, a little lassitude, dyspnea upon exertion, and a heart murmur of increasing intensity. Two such cases have been followed by the writer for a period of several years. The first is that of a boy of eight years whose only symptoms were those just described. A blood culture was made and *Streptococcus viridans* isolated. Careful examination of his case showed a small discharging sinus above a canine tooth, which led to a necrotic second tooth. This was removed and the cavity curetted, and the child recovered, except for the damage to the mitral valves. At the end of four years the boy is alive and well and has withstood without undue stress a recent attack of pneumonia. The second case, in which the symptoms were merely those of recurrent afternoon temperature, lassitude, pain in the legs, and recurrent crops of petechiæ around his ankles, also showed the *Streptococcus viridans* in the blood culture. He continued under observation nearly two years, and then removed to another part of the country.

A third patient with viridans infection made a definite clinical recovery after six weeks in hospital, but in his case the onset was acute, with severe tonsillitis and pharyngitis, a subsequent polyarthritis, and the appearance of a scattered erythematous eruption which might have been an erythema from drugs, as the patient had received generous doses of salicylates before admission. A loud mitral systolic murmur was present. In this instance the blood culture gave a feeble growth of the *Streptococcus viridans,* and while the value of intravenous injection of sulphate of magnesia was under discussion his temperature fell and he made a rapid recovery.

In the prolonged cases the symptomatology is so varied as to be difficult of classification. Owing to the variation in the parts of the body which may be affected by septic emboli, there may be at one time predominating symptoms of some special organ, as of acute renal disease. The formation of a renal infarct may be heralded by deep lumbar pains, chills, partial or complete suppression of urine, hematuria, and the presence of varying amounts of albumin, blood-casts and, as the acute condition subsides, both hyaline, coarsely and finely granular casts. Infarction of the liver may cause subcostal pain and tenderness, dull backache, and a varying degree of jaundice; the circulation may reflect the depressing qualities of a biliary poisoning; the blood-pressure may fall and the pulse become slow and compressible, and there may be drowsiness and lethargy. The spleen is sometimes affected and becomes enlarged and hard. With the further progress of the disease the anemia becomes profound. It is of the secondary type and is steadily progressive. As the anemia becomes more profound, edema is not uncommon. This apparently is not dependent upon the degree of cardiac involvement, and may affect the face first, even suggesting pernicious anemia at first glance. Pulmonary embolism may give rise to pain, hemorrhage and signs of pulmonary consolidation; or hypostatic pneumonia may appear. The two types of skin lesions have been mentioned. Described more in detail, they consist, first, of small reddish-purple spots, 1 or 2 mm. in diameter, or sometimes a little larger, that appear usually about the ankles and over the dependent portion of the leg below the knee. They may vary from a few scattered spots to a densely speckled area of considerable size. They are not sensitive, do not disappear under pressure, and tend to recur in crops. Some authors describe a somewhat larger petechial eruption occurring about the wrists, elbows, ankles, and knees that is distinctly pink, slightly raised, and varies from 5 to 10 mm. in diameter. Osler calls attention to the frequency with which larger nodules are found in cases of chronic endocarditis. This lesion is a tender, raised, reddened area shading off at the edges, and occurring singly or occasionally in groups, usually about the larger joints, though they have been observed on the thighs, arms and trunk. Such spots may average from 2 to 4 mm. in length by from 1 to 3 in breadth. They are occasionally much larger, and are regarded as septic emboli deposited in the capillaries of the skin. The writer has observed them to appear coincidentally with chills and a considerable rise in temperature.

Differential Diagnosis of Malignant Endocarditis.—The protean manifestations of chronic endocarditis are such as to make its diagnosis extremely difficult. It may simulate typhoid fever, pneumonia, cerebrospinal meningitis, tuberculosis, exophthalmic goiter (acute febrile variety), malaria and rheumatic fever.

TYPHOID FEVER.—In the early diagnosis it may be impossible to distinguish endocarditis from typhoid fever until a positive blood culture or a positive Widal can be obtained. There is usually leukocytosis, while typhoid usually shows leukopenia; the temperature curve may be identical. The early appearance of a murmur in a previously negative heart is also suggestive. It may be impossible to make a diagnosis within the first week or ten days, but an enlarged spleen, slow pulse, leukopenia and negative heart suggest typhoid. Repeated blood cultures may be necessary.

RHEUMATIC FEVER.—Many cases have their inception in a definite rheumatic fever, and it may be several weeks before suspicion is directed to the predominance of the endocardial factor. An unusual temperature range, with more than ordinarily rapid anemia, the evidences of profound toxemia as indicated by the patient's appearance and general morale, suggest the malignant factor. If in addition we find an enlarged spleen and a petechial eruption, the diagnosis should be clear.

MALARIA.—The absence of the plasmodia, the presence of a leukocytosis, positive heart-sounds, and a positive blood culture make the diagnosis fairly certain.

MILIARY TUBERCULOSIS.—This diagnosis may be extremely difficult until a positive blood culture can be obtained. As a rule, the leukocytosis is lacking in tuberculosis, or else there is an excessive lymphocytosis, but the absence of physical signs in the chest, the failure to find tubercle bacilli, a persistent temperature, and the progressive toxemia may make differential diagnosis impossible until repeated blood cultures demonstrate the organism, or progressive endocardial changes serve to identify the heart condition.

PNEUMONIA.—One may depend upon the conjunction of rapid pulse, increased respirations, and high temperature, even without physical signs, to suggest pneumonia rather than endocarditis. A positive blood culture, the presence of petechiæ, and increasing heart murmurs should be sufficient to exclude pneumonia.

SPINAL MENINGITIS.—Lumbar puncture with a high cell-count and the presence of the meningococcus, and a positive Kernig and Babinski, should serve to identify meningitis. A positive blood culture completes the picture.

EXOPHTHALMIC GOITER (the acute febrile type of Graves' disease).—The comparative rarity of this condition, positive ocular symptoms, a tender and large thyroid, and a negative blood culture indicate the thyroid origin.

Another occasional manifestation is the cerebral or embolic form of endocarditis. The question will arise here between an embolism due to the breaking off of an old vegetation, embolism from the uterine sinuses, from a fracture or operative wound, or from thrombophlebitis on the one hand, or a septic embolus of cardiac origin on the other. The question of *prognosis* here hinges on the nature of the embolus. The writer has seen one case of embolism immediately following labor, without previous history other than vague toothache pains and some malaise. The *Streptococcus viridans* was demonstrated in the blood-stream, and death occurred on the seventh day. The blood culture offers the only means of differential diagnosis in such a condition.

Treatment of Malignant Endocarditis.—GENERAL MANAGEMENT.—The treatment of malignant endocarditis has thus far proved most unsatisfactory. The measures employed include hygiene, physiotherapy, vaccine and serum therapy and drugs. As a certain very small proportion of the cases recover spontaneously, it is essential that every effort should be employed to increase the patient's strength, so that his own powers of resistance may be fortified and supported, in the hope of eventual recovery. Absolute **physical rest, freedom from mental irritation** and an easily assimilated **diet,** sufficiently rich in calories to meet the needs of the body without taxing the digestive system, are the first essentials. If there is evidence of interference with nitrogen excretion, a low protein diet is indicated, otherwise a considerable choice in the articles of diet is permissible. Hyperpyrexia should be met by **tepid sponging** with water or alcohol; abundant **ventilation** is essential and the patient should not be too warmly wrapped.

HYPODERMATIC TREATMENT.—*Solutions.*—Two distinct forms of treatment by the subcutaneous and intravenous routes have been employed. The first includes **intravenous injections** of a variety of substances including a 10 to 20 per cent. solution of **magnesium sulphate, Dakin's hypochlorite solution,** a combination of **guaiacol** with **sodium salicylate,** and the latter drug alone. Normal **saline solution** and **sodium bicarbonate** solution have been tried, also **salvarsan, diarsenol,** and **sodium cacodylate.** While individual reports of each one of these methods have claimed marvelous results, it is noteworthy that each has been equally condemned by subsequent investigators. Hirschfelder reports a thrombosis following infusion of Dakin's solution, and the writer has had the opportunity to record the death of a patient previously reported improved by the use of sulphate of magnesia. The method of injecting considerable doses, e.g., 40 grains (2.60 grams) of sterilized sodium salicylate intravenously has been tried out side by side with a number of control cases in a series of patients suffering from acute rheumatic fever, and no advantage has been noted, although Conner reports excellent results in his series. As in nearly all cases of this disease the myocardium is weakened and the heart is already staggering under the combined load of intoxication and muscular weakness, it is patently illogical to load the circulation directly with more fluid, especially as only those germs are directly reached that are floating in the blood stream. Those that are protected beneath the surface of the thrombi, or hidden away within the heart-valves, are not reached, nor could they be affected by a solution so dilute as to be harmless to the general system.

Vaccine and Serum Therapy.—**Vaccines** have been extensively employed. Autogenous and stock vaccines have been tried, and each have their advocates. The writer's experience tallies with that of Libman, Hirschfelder and others, whose reports are thus far discouraging. If any cases are suitable for vaccine therapy it would seem that the chronic types of malignant endocarditis are particularly so. But thus far a variety of vaccines from several sources have proved entirely inadequate. In course of time results may be obtained by combinations of bacteria and by continued effort, and further observations are essential before the method should be entirely condemned.

Combined streptococcus serum should have a thorough trial, as a few favorable reports of the serum treatment of influenza-pneumonia seem to indicate that the method has positive value.

PROPHYLAXIS.—As it is possible, if not probable, that fresh accessions of bacteria are constantly entering the blood stream from some point of focal infection, it is essential that every such point should be sought out and removed. **Carious teeth** should be **extracted**, apical granulomata should be sought for with the *x*-ray (which for dental purposes can be readily brought to the bedside) and extracted. Evident pus foci in the **tonsils** should be **relieved** and, in cases of rheumatic infection, infected tonsils should be **removed** as soon as recovery is sufficiently advanced. In cases of the milder type of chronic ulcerative endocarditis, it may be advisable to remove the tonsils even in the presence of active disease, following the precedent set in the care of tuberculous patients with infected tonsils. The treatment of the appendix and gall-bladder are surgical problems that may enter into consideration if definite infection from either one is demonstrable.

MEDICINAL TREATMENT.—**Digitalis**, a much abused and most valuable therapeutic agent, is warmly recommended by some, and is condemned by others. The use of digitalis in ulcerative endocarditis must depend upon the condition of the myocardium. As the main object of the treatment is to support the patient, digitalis is certainly indicated when the heart shows signs of fatigue. It may properly be given in small tonic doses—5 minims (0.3 c.c.) of the standardized, fat-free tincture—before symptoms of this nature arise, as a means of supplying definite support, as a prophylactic factor, and as a means of inducing digitalism while the heart is still capable of prompt response. The condition may be considered somewhat analogous to pneumonia, in which modern teaching insists upon getting the heart-muscle well under the control of digitalis as early in the disease as possible. The use of digitalis must be one for individual judgment to decide in each case. **Salicylates** of all varieties have been warmly recommended, but do not seem to influence the course of the disease. Other heart stimulants may be desirable to whip up a flagging circulation or to produce temporary tiding over of a crisis. In cases where the kidney becomes involved **hexamethylenetetramin**—grains 5 (0.324 gram)—may be helpful in controlling the local infection. The **theobromin salts** are useful to increase excretion, and **caffein-sodium benzoate**—grains 5 (0.324 gram)—in full doses combines a stimulating effect upon both heart and kidneys.

Prognosis.—The outlook in all cases of this form of infection is distinctly bad, although recoveries are possible. The writer reported 3 cases of recovery from bacteriemia of the *Streptococcus viridans* variety (Long Island Med. Jour., Oct., 1918), and doubtless there are others that have passed unrecorded or unrecognized. Even in patients who have youth and vigor and a clean health record and in whom the infection seems at first to be very mild, the disease most frequently progresses steadily to a fatal termination in spite of everything that can be done.

Occurrence and Distribution.—T. J. Horder's statistics, taken from the records of St. Bartholomew's Hospital, show 150 cases among 19,904 patients. The greater number occurred between the ages of fifteen and fifty, as follows:

Fifteen to twenty	29	cases
Twenty to thirty	39	"
Thirty to forty	31	"
Forty to fifty	23	"
Under five years	2	"
Five to ten	5	"
Fifty to sixty	8	"
Over sixty	4	"

The incidence was about equally divided between the sexes.

IDENTIFICATION OF MURMURS

For convenience of reference a brief tabulation of the main characteristics of the principal murmurs is appended. This is intended merely as an aid in identifying the affected valve, and is in no sense a complete discussion. The reader who desires a full discussion of the late and remote effects of chronic valve changes is referred to the appropriate articles on chronic valvulitis.

Mitral Regurgitation (Mitral Insufficiency or Incompetency)

Frequency.—Alone it comprises about 50 per cent. and combined with other valves about 65 per cent. of all valvular defects. These figures vary surprisingly little, being almost identical for European and American clinics.

Place.—The murmur is heard at the apex, is transmitted to the axilla, and is audible behind along the border of the left scapula at about the level of the second and third dorsal vertebræ. Not infrequently it may be traced along a curved line extending from the apex to the left border of the sternum and thence up to the pulmonary area.

TIME.—The murmur is systolic.

QUALITY.—At first it is apt to be soft and blowing, gradually becoming louder, harsher and more rasping. At times it is distinctly musical. Its wide variations in pitch, intensity and quality have led to the use of numerous descriptive terms depending upon the fancy of the observer.

THRILL.—A systolic thrill is frequently palpable over the apex.

OTHER SIGNS.—The second pulmonic sound is regularly accentuated in mitral regurgitation, especially if the right ventricle has had time to hypertrophy.

Mitral Stenosis

FREQUENCY.—In acute endocarditis it is seldom seen, as it is essentially a sclerotic change. When noted it is usually in a case of reïnfection or of a recent acute infection engrafted on a preëxistent valvulitis. Mitral stenosis alone furnishes from 8 to 10 per cent., and combined with other lesions about 25 per cent., of valve defects.

PLACE.—The murmur is heard over an area usually no larger than a half-dollar, just to the sternal side of the apex.

TIME.—The murmur is presystolic. It begins toward the end of diastole, grows louder, and ends abruptly with the beginning of the first sound.

QUALITY.—"Rumble" describes the sound accurately. The first sound has a short, snapping quality; the second sound is apt to be faint; and, unless timed by the impulse, the second sound may be overlooked and the first mistaken for it.

THRILL.—A *presystolic* thrill, palpable over an area of two or three cm. to the right of the apex, is also characteristic.

OTHER SIGNS.—The apex impulse is short and abrupt and retraction of the chest-wall in the fourth interspace can be seen during systole.

Aortic Regurgitation (Aortic Insufficiency or Incompetency)

FREQUENCY.—Alone, about 20 per cent.; combined with other lesions, about 45 per cent.

PLACE.—Point of greatest intensity over an area about the center of the sternum at the level of the second cartilage. It can be traced downward to the left and into the left axilla.

TIME.—Early diastole.

QUALITY.—The sound varies from a faint whiff or "dying sigh" (Mackenzie) to a loud, harsh or hissing murmur.

OTHER SOUNDS.—Flint's murmur—a presystolic rumble heard at the apex—accompanies a moderate percentage of cases of aortic regurgitation. A third heart sound has been described by Thayer. It is a sharp, loud, well-defined sound coming just at the end of the diastolic murmur. The first heart sound has a snapping quality in one-third of the cases.

Aortic Stenosis

FREQUENCY.—About 5 per cent. of all heart murmurs. Rare in acute form, unless already present before an acute attack.

PLACE.—The murmur is heard over practically the entire precordium, with its maximum intensity over the first right interspace at the edge of the sternum, as well as over the carotids. The second sound is frequently diminished and sometimes absent.

TIME.—It begins just after the beginning of systole, and ceases with valve closure.

QUALITY.—The murmur has a loud, rushing quality, sometimes audible at a distance from the chest-wall.

THRILL.—A systolic thrill is usually palpable over the entire heart, but most marked over the aortic area.

Tricuspid Regurgitation (Insufficiency or Incompetency)

FREQUENCY.—Some degree of tricuspid regurgitation exists in almost every case of weakness of the right side of the heart, so that as a functional condition it is extremely common. As an organic lesion, on the other hand, it is rare, comprising less than 1 per cent. of organic valvular lesions.

PLACE.—The murmur is heard over the lower part of the sternum and the ensiform cartilage. It is also heard to the right of the sternum over the cartilages of the sixth and seventh ribs, and over a corresponding area, but a little larger, to the left, as well as in the intervening spaces.

TIME.—The murmur is systolic, accompanying the first sound throughout. It is heard most distinctly and loudly to the left of the sternum, while on the right the sound assumes a shorter and sharper character.

THRILL.—Occasionally a systolic thrill can be felt over the area described above.

OTHER SIGNS.—Venous pulse. The veins of the neck show a full, large pulsation coincident with the carotid pulse. The liver is apt to be large and pulsating.

BIBLIOGRAPHY

BABCOCK, ROBERT H. Diseases of the heart and arterial system. D. Appleton & Co., 1909.

COLE, RUFUS I. Experimental streptococcus arthritis in relation to the etiology of acute articular rheumatism. Jour. Infect. Dis., Chicago, 1904, i, 714.

——— The etiology of acute articular rheumatism. New York Med. Jour., 1906, lxxxiii, 534.

HIRSCHFELDER, ARTHUR DOUGLASS. Diseases of the heart and aorta. Third Edition Revised, pp. 398-419. Bibliography page 419.

HORDER, T. J. Infective endocarditis. Quart. Jour. Med., Oxford, 1909, ii, 289.

LIBMAN AND CELLER. Am. Jour. Med. Sc., 1910, cxl, 516.

LONGCOPE, E. T. Experimental arthritis and endocarditis produced by a streptococcus isolated from the blood of a case of rheumatism, endocarditis, and chorea. Am. Jour. Med. Sc., Phila., 1904, cxxviii, 601.

MacKenzie, Sir James. Diseases of the heart. Oxford University Press, 1918.

Osler, W. Chronic infective endocarditis. Quart. Jour. Med., 1909, ii, 219.

Poynton, F. J., and Paine, A. The etiology of rheumatic fever. Lancet, London, 1900, ii, 861.

——— Some further observations upon rheumatic fever. *Ibid.*, 1901, i, 1260.

——— The present position of the bacteriology of rheumatic fever. Brit. Med. Jour., London, 1901, ii, 779.

——— The pathology of rheumatism. Practitioner, London, 1901, lxvi, 22.

——— Arthritis: A comment upon and review of some recent literature upon the subject. *Ibid.*, 1903, lxxi, 128.

Price, Frederick W. Diseases of the heart; their diagnosis and treatment by modern methods; with a chapter on the electrocardiograph. H. Frowde, London, 1918.

CHAPTER III

CHRONIC VALVULAR DISEASE OF THE HEART

By Thomas F. Reilly, M.D., F.A.C.P.

Introduction, p. 91.
Aortic stenosis, p. 93:—Etiology, p. 93; Symptomatology, p. 93; Diagnosis, p. 96; Prognosis, p. 97; Pathology, p. 98.
Aortic insufficiency (Aortic regurgitation), p. 97:—Etiology, p. 99; Symptomatology, p. 100; Diagnosis, p. 106; Treatment, p. 107; Prognosis, p. 109; Pathology, p. 111.
Mitral regurgitation, p. 112:—Etiology, p. 112; Symptomatology, p. 113; Diagnosis, p. 120; Prognosis, p. 123; Pathology, p. 126.
Mitral stenosis, p. 127:—Etiology, p. 127; Symptomatology, p. 128; Diagnosis, p. 134; Complications and sequelæ, p. 139; Prognosis, p. 141; Pathology, p. 144.
Tricuspid regurgitation, p. 146:—Etiology, p. 146; Symptomatology, p. 147; Differential diagnosis, p. 148; Prognosis, p. 148; Pathology, p. 149.
Tricuspid stenosis, p. 149:—Etiology, p. 149; Symptomatology, p. 149; Diagnosis, p. 149; Prognosis, p. 150; Pathology, p. 151.
Pulmonary stenosis, p. 151:—Etiology, p. 151; Symptomatology, p. 151; Diagnosis, p. 151; Prognosis, p. 152; Pathology, p. 152.
Pulmonary regurgitation, p. 152:—Etiology, p. 152; Symptomatology, p. 152; Differential diagnosis, p. 153; Prognosis, p. 153; Pathology, p. 154.
General prognosis of chronic valvular disease, p. 154:—Cause of cardiac lesion, p. 156; Kind of person who has heart disease, p. 158; Conditions affecting the prognosis, p. 160.
General treatment of valvular disease, p. 164:—Cases discovered by accident and presenting no symptoms, p. 164; Outline of treatment, p. 166—Cases presenting minor symptoms accompanying valvular disease, p. 166:—Special indications, p. 169; Outline of treatment, p. 171—Individual symptoms and their treatment, p. 172—Broken compensation:—Diet, p. 184; Hope, p. 185; Digitalis, p. 185; Other preparations of digitalis, p. 188; Substitutes for digitalis, p. 189; Indications for the use of digitalis, p. 190; Contra-indications to the use of digitalis, p. 190; Opium, p. 191; Other drugs of use in cardiac disease, p. 192; Therapeutic measures other than drugs, p. 195; Outline of treatment in decompensation, p. 200.

Introduction.—About 5 per cent. of all patients met with in general practice have chronic valvular disease of the heart. This percentage is much larger in hospital practice, wherein it reaches from 10 to 15 per cent., depending upon the nature of the service, *i.e.,* whether it is an ambulance service or a selective service. The results of many thousands of examinations of school children by the Health Department of New York show that more than 1 per cent. suffer from serious chronic valvular disease. During the last decade the attention of the profession has been directed more particularly toward the study of the muscles of the heart than of the valves. Any one who has seen, at autopsy, the hard and sclerotic valve, which is sometimes even calcareous throughout and which, however, must have functioned for years in that condition, cannot help being struck with the idea that it requires more than a damaged valve to produce a break in compensation. This added factor is the muscle of the heart, and upon it, more than upon the condition of the valve, depends the ultimate basis of the patient's outlook for life. The demonstration of Aschoff's bodies in the muscle of the heart in the course of rheumatic infection, proving that such bodies are the foundation of a later specific sclerosis in the muscle and that they are coincident with vegetative involvement of the edges of the valves, has gone far to confute the opinion that the infection involves the valves alone, and has indicated that it commonly involves the whole heart when any portion of it is involved. For that reason the importance of the physical signs of endocarditis is largely indirect. The signs of valvular disease prove that one part of the heart has certainly been damaged by some agent, and that it is almost certain that other portions of that organ are likewise involved. Unfortunately, in the vast majority of cases, we have no other physical means of estimating what the nature of the damage done has been, except by auscultation of the valve sounds. One must hasten to add that symptoms are of far more import from a diagnostic and prognostic standpoint than are any or all of the physical signs, and that when they are well marked, they are our best guide in arriving at any conclusion. However, unless there is something definitely diagnostic in these phenomena, in the absence of physical signs, one cannot, in the early stages of diseases, give a positive opinion as to their organic significance. For instance, dyspnea, the cardinal symptom of heart-failure, may be due to the diseases of the lungs, blood or mediastinum, and in the absence of some indication of a physical change in the heart there is no way of arriving at a conclusion. Irregularities of the heart-beat indicate that there may be some degeneration of the muscle. Irregularities which can be of diagnostic or prognostic import early in the course of the disease are comparatively uncommon in proportion to the total number of cases of cardiac involvement. The elucidation of the odd and unusual irregularities can only be accomplished by instrumental means in hospitals and institutions in which much time can be devoted to solving these problems. In any event the net result is almost always academic rather than practical. It is safe to say that, with the exception of auricular fibrillation, the number of such cases presenting nothing but the evidence of damage to a muscle, as revealed on a pulse-tracing or electrocardiogram, are negligible, as compared with the number of patients suffering from endocarditis and myocarditis.

The necessity for a study of the valve-sounds is especially evident in children, because here information as to the muscle condition is rarely obtainable through tracings. In more than 80 per cent. of the patients presenting evidence of broken compensation some abnormality of the valve sounds will be found which can be described in an intelligible manner and which can be evaluated by the practitioner. For this reason study of the condition of the valves, as determined by the practitioner by ordinary physical means, is the best objective index which we have at the present time of the conditions existing in the heart.

It is frequently argued that the close differentiation between the various valve lesions has only an academic value, and that after all the absence of loss of compensation is the important feature. While this is true to a certain degree in well-marked and advanced cases, such as are commonly seen in hospital practice, there are essential differences in the symptomatology, and especially in the prognosis of early and moderately advanced cases, which render the close study of the individual valve symptoms a necessity.

AORTIC STENOSIS

Etiology.—Aortic stenosis as an uncomplicated lesion is very rare. In a large hospital service it occurs once or twice a year and is a curiosity. As a combined lesion, however, in association with aortic regurgitation, it is not so rare; yet here the associated lesion commonly masks the signs and symptoms of stenosis. It is present in about one-half of one per cent. of all cardiac valvular lesions. When found as an isolated lesion it is rarely due to rheumatic fever, but is commonly associated with arteriosclerosis. Most of the supposed aortic stenoses in which the diagnosis is made on the strength of the presence of an aortic systolic murmur before the patient is fifty years of age are due to changes in the blood, producing hemic murmurs, while most of those made in patients over fifty years of age are due to arteriosclerotic changes in the aorta. Aortic stenosis is far more common in men than in women, and is rarely apparent before middle life. It is due either to a previous attack of endocarditis or to a degenerative process. When it is due to endocarditis there is usually a concomitant involvement of the mitral valve.

Symptomatology.—These patients rarely complain of symptoms which are in any way characteristic of the disease. As in all basal affections of the heart, there is a sense of constriction or pain over the second right costal cartilage which is referred to the back. This is most common in the cases due to degenerative lesions. If the cause of the lesion is a former attack of endocarditis the symptoms do not appear for many years after the original disease. Of the minor symptoms, *dizziness* and *vertigo* are more commonly present than is the case in any other valve lesion. These are the symptoms which most frequently call attention to the lesion. Old people especially complain of these manifestations on lying down and getting up quickly. In the case of men they are most noticeable when the barber's chair in which they are lying is being raised or lowered. This is due to cerebral anemia. Occasionally fainting attacks occur and are due to the same cause. In estimating the significance of these symptoms occurring in conjunction with a systolic aortic murmur, one must always keep in mind the fact that they may be due to other causes, such as cerebral arteriosclerosis associated with a roughened aorta. When there is any failure in compensation, however, the associated functional mitral insufficiency is responsible for the symptoms. This manifests itself commonly as shortness of breath on exertion. As the patient is usually well advanced in life by this time it acts as a red light of danger, warning him of the limitation of his activity, and thus prevents undue dilatation. For this reason careful living may prolong life for many years after the discovery of the lesion.

PHYSICAL SIGNS.—*Observation.*—Observation seldom reveals anything, because at the time of life at which the lesion becomes apparent, even if the heart does enlarge, the chest-wall is so rigid that it does not expand enough to render the enlargement noticeable.

Palpation.—A systolic thrill over the base in the second right intercostal space near the sternum is commonly present, although it is not pathognomonic, as it is often associated with other cardiac or vascular diseases. The apex-beat, when it can be felt at all, is seldom noticeable beyond the nipple line, and is usually in the sixth intercostal space. However, more often the apex-beat is *missing*, and this absence is a startling phenomenon. When it happens in any chest examination it calls for a careful scrutiny as to the cause.

(*a*) *Pulse.*—The pulse is slow, small, hard and regular. It is seldom more than 60 to the minute. It is frequently quite characteristic, and is often the sole deciding factor in determining the diagnosis. The wave is greatly prolonged and it seems to the examiner as though it would never drop. The artery is generally quite full between beats. This is due to the relatively small size of the aortic orifice, which permits only a small amount of blood to pass through at any one time, so that in order that the ventricle may empty itself a longer period of systole is necessary.

Percussion.—It is frequently difficult to map out the size of the enlarged heart by percussion because of the emphysema which so often accompanies this lesion in old people. This emphysema also accounts, at times, for the absence of the apex-beat.

Auscultation.—The systolic murmur so commonly heard at the base of the heart and transmitted up into the vessels of the neck is the least dependable, from a diagnostic standpoint, of any of the murmurs associated with valvular disease of the heart, because it is more often due to changes in the wall of the aorta than to changes in the valves themselves. It is heard with maximum intensity just outside of the right edge of the sternum in the second intercostal space. Occasionally, if one moves the stethoscope downward from the point of maximum intensity along the sternum, the murmur is lost over the body of the right ventricle. When the stethoscope is moved along to the apex the murmur may be heard here if hypertrophy is present. This is due to the transmission of the sound along the muscles of the left ventricle down to the apex where they come close to the chest-wall. This is, however, a rather uncommon phenomenon. It has been asserted that this murmur at the apex disappears when pressure is exerted with the stethoscope. It must be differentiated from mitral regurgitation by other signs. When true aortic stenosis exists the murmur is not only transmitted up the aorta, but is usually heard on the right border of the sternum as far down as the fourth rib. The murmur is long drawn out and is of a hissing character. The first sound of the heart is usually absent at the base, the bruit taking its place. When the murmur is loud it may be heard at a greater distance from the chest-wall than any other murmur. The nature of the aortic second sound is of more value diagnostically than the presence of the murmur itself. It is a very faint sound (often absent altogether), and can scarcely be heard, due to the fact that the valves cannot close tightly together; consequently, an accompanying aortic regurgitation is most always present. If a good strong second aortic sound is present, the observer is justified in believing that the systolic murmur is due to changes in the aorta and not in the valves.

The first sound at the apex, when it can be heard, is dull and prolonged, and may be accompanied by the systolic murmur mentioned above, which has been transmitted down along the ventricle to the apex. When a true systolic murmur at the base is accompanied by the above-mentioned signs at the apex in a young person, the diagnosis of aortic stenosis is warranted. After middle life this rule does not always apply. In such a case the presence of an accentuated second aortic sound instead of a weak or missing second sound would indicate atheroma and dilatation of the aorta rather than aortic stenosis.

Special Examinations.—*Blood-pressure.*—There are no characteristic changes unless there is associated arterial disease or aortic regurgitation, in which instances the pressure is usually higher than normal.

Sphygmograph.—In well-advanced cases the tracing is pathognomonic; it shows a pulse of small amplitude, the percussion wave is oblique, and the summit is gradually attained and continues much longer than normally. It is called the anacrotic pulse-tracing. A somewhat similar form, the pulsus bisferiens, is sometimes present, but it is not as characteristic as the anacrotic. When aortic regurgitation is also present this pulse-tracing is not so definite.

Electrocardiograph.—The R-wave of the electrocardiogram is directed downward in lead 3. This is not diagnostic of aortic stenosis, but shows the presence of a left ventricular hypertrophy, which is always present, and which, in conjunction with other signs, is helpful in arriving at the diagnosis.

X-ray Examination.—The orthodiagram shows enlargement of the heart-shadow to the left. The lower portion produces the appearance of a horizontal oval above which the shadows of the pulmonary artery and of the aorta are quite visible. The shadow in general resembles that present in aortic regurgitation, but is smaller than is usually the case in uncomplicated instances of the latter lesion.

Diagnosis.—Greater care must be exercised in the diagnosis of this than of any other valvular lesion. The region at the base of the heart has been well named the region of romance in diagnosis. The most common error is to diagnose a condition as aortic stenosis because of a roughening of the aorta which produces a basal systolic murmur transmitted up into the vessels of the neck. Such a murmur is a very common finding in patients over fifty years of age. The character of the murmur is the same as that of aortic stenosis. There is, however, an absence of the other signs associated with aortic stenosis, such as hypertrophy, feeble second aortic sound, and characteristic pulse. In the cases of sclerosis of the aorta associated with a systolic murmur, on the contrary, one finds that the aortic second sound is loud, clanging and accentuated, due to the increase of arterial tension associated with general arterial sclerosis. The feeble or absent second aortic sound of aortic stenosis is due to the stiffness of the aortic segments and their slow recoil which follows the relatively slow distention of the arteries. A history of rheumatic fever or of syphilis would indicate aortic stenosis rather than arteriosclerosis of the aorta as a cause. An acute *aortitis* may be confusing when seen for the first time. It produces a similar murmur; it is commonly associated with substernal oppression or a pain radiating out into the shoulder, and with dyspnea on slight exertion. There is a marked accentuation of the second aortic sound, and a more rapid pulse. Similarly, in rare instances, a dilatation of the aorta due to any cause may be accompanied by a basal systolic murmur. In such cases there is a dullness at the base, and a clanging accentuated second sound.

Hemic murmurs are frequently responsible for basal systolic bruits. These hemic murmurs accompany the first sound and do not take its place. They are often multiple and can generally be heard over the larger vessels throughout the body, if pressure is applied over them with a stethoscope. It is seldom that such a murmur is as loud as is that of aortic stenosis. A murmur of similar character to that of the hemic murmur is present in the asthenia of acute disease, and it is particularly common under such conditions in small children. More than 20 per cent. of small children with a continued temperature show some such systolic basal murmur. This disappears during convalescence. It is not far transmitted, nor are any other characteristics of aortic stenosis present. Its origin is similar to that of the hemic murmur, and it is of no evil consequence.

A mediastinal tumor may cause pressure on the aorta and thus be responsible for an aortic systolic bruit that is transmitted up the vessels of the neck. In such instances there is an enlarged area of dulness at the base; there is no alteration of the second sound, nor displacement at the apex.

Pulmonary stenosis produces intrinsically the same physical signs on palpation and auscultation as does aortic stenosis. It is a disease of youth and is almost always congenital or associated with some other lesion. It is not often a cause of difficulty in diagnosis. The chief point in differentiation from the standpoint of physical signs is the fact that the murmur is not transmitted up the arteries of the neck. It can best be heard to the left of the sternum rather than to the right. The pulse is decidedly different, and there is hypertrophy of the right ventricle, whereas in aortic stenosis there is hypertrophy of the left.

When the aortic stenotic murmur is very loud and is heard quite distinctly at the apex it may be a question whether this is transmitted from the base or whether a secondary mitral regurgitation is present. If the latter is the case the condition is usually a relative mitral regurgitation, and other evidences of broken compensation will be present, especially the complaint of dyspnea on slight exertion. If a true organic lesion is also present in the mitral valve, a gradual diminution of the apical murmur will be noted on moving the stethoscope upward from the apex toward the base, and about the third interspace the basal systolic murmur will begin to appear.

The accentuated second pulmonic sound of mitral disease is of great diagnostic value in such instances and usually there are other evidences of mitral disease as well.

When the murmurs of aortic stenosis and aortic regurgitation are both heard the question often arises as to whether a true stenosis is present or whether the murmur is due to the thickened, roughened valve of aortic regurgitation. If the pulse is sudden or collapsing there is no room for doubt that the lesion is regurgitation, and this is by far the commonest condition. In the absence of such a pulse one is justified in feeling that stenosis is the predominating lesion. Finally, to recapitulate, there are four findings which are requisite as a basis for the diagnosis of aortic stenosis. Three of these should certainly be present: First, a systolic thrill at the base; second, a slow lazy pulse, and third, a systolic murmur best heard at the second right costal cartilage and transmitted up the vessels of the neck and usually down the right side of the sternum, and fourth, a faint or scarcely noticeable second aortic sound.

Prognosis.—In general the prognosis depends upon the cause. In a well-developed case in a young adult, where there is no question as to the diagnosis, the lesion is usually a progressive one, and death is at most only a matter of a year or two. The average duration of life in aortic stenosis, from the time of its recognition, has been placed at four years. According to Broadbent the average age of death in such patients is forty years. In the cases which develop late in life as the result of sclerosis (and these are the most common type) the outlook is very much better. The luetic cases, if recognized before the onset of symptoms, are curable. After the symptoms have appeared, little is to be hoped for in the way of permanent improvement. If there is a coincident involvement of the mitral orifice the prognosis is much worse. When the disease is combined with aortic regurgitation, as is so often the case, the course of the latter determines the prognosis. The immediate outlook depends (1) upon the degree of stricture, as determined by the character of the pulse, and (2) upon the condition of the muscle, as determined by the presence of symptoms, such as pain, dyspnea, etc. When the heart is not enlarged and the apex is in the right location, there is no cause for alarm. The same holds true if no subjective or objective symptoms are present after moderate exertion. In these favorable cases the pulse is slow and regular, and the pulse-wave is typical. The presence of auricular fibrillation in the sclerotic form is more serious than in other valvular lesions, inasmuch as it does not react to digitalis and the patient does not long survive its onset. Repeated attacks of fainting, dyspnea on exertion and marked dullness of intellect are strongly suggestive of approaching loss of compensation. These mental disturbances are quite common even a year before there is decided loss of compensation. The cases of aortic stenosis associated with anginal attacks, or with pain on exertion, are distinctly serious, no matter what the original cause of the lesion may be. It is true that some of these patients survive such attacks for a few years, but they are apt to die suddenly. In a fair percentage of cases, young patients suffering from aortic stenosis develop fatal pulmonary tuberculosis. In general, the subjects of aortic stenosis are always living up to the limit of their endurance, as it were, and have reserve of energy to draw on in an emergency, such as follows extra exertion or an infectious disease. When such an event occurs and compensation begins to fail, rest and medicines do not put the patient on his feet again, as is the case with other lesions, and the progress is steadily downward from the time of the appearance of the first definite symptom.

Pathology.—The lesion is either the result of a previous endocarditis or is due to sclerosis. In the endocarditic form there is a thickening of the valve edges, and organization of the vegetation which is present, and finally sclerosis. Later on in life infiltration with calcareous material takes place, and the orifice may be a rigid ring instead of a valve. In the arteriosclerotic form, which is by far the most common, and which is part of a general arteriosclerosis, the changes which take place in the valves are similar to those taking place in the inner coat of all the blood-vessels in that individual. Not infrequently on postmortem such valves feel hard and sclerosed, and yet there is no apparent stenosis. Hypertrophy of the left ventricle is marked, but is less evident than in regurgitation. At first concentric hypertrophy is present. Later dilatation appears. Because of the contraction of the orifice the ventricle is not able to expel all the blood which it contains during systole. After each succeeding diastole blood is left from the preceding contraction, thus causing a more strenuous systole than before. This accounts for the early hypertrophy. In addition the smaller size of the orifice causes systole to be greatly prolonged in its effort to expel as much blood as possible, and this accounts for the continued pulse-wave. When the muscle cannot overcome these factors dilatation of the left ventricle must result, and relative mitral regurgitation is the usual consequence.

AORTIC INSUFFICIENCY (AORTIC REGURGITATION)

Etiology.—Aortic insufficiency is the commonest lesion at the aortic orifice. It is present forty times as frequently as aortic stenosis, and it is much more common in males than in females. It is a disease of middle age. Osler has well said that the causes of this disease may be symbolically represented by Venus, Vulcan and Bacchus. According to statistics collected in many large cities, at least 75 per cent. of the cases are due to lues. This percentage does not hold true for all localities, but certainly more than one-half of all cases are luetic, and it is well to regard lues as the cause until otherwise proven. This is even more markedly true among negroes than among whites. The reason for this affinity of lues for the aortic orifice is not always clear, but inasmuch as in 50 per cent. of all cases of lues there is some involvement of the circulatory organs and as involvement of any structure in the body by lues is in direct proportion to the amount of stress or irritation to which it is subjected, this relative percentage of vascular disease occurring in the course of lues may be conveniently remembered by associating it with rheumatic fever which affects the adult heart also in 50 per cent. of the cases. The tissues of the aortic orifice are most commonly affected because they are constantly under strain and tension.

Visible evidences of this traumatic predilection of lues is found in the eruptions, which are most commonly visible in the skin at the hat-band, wristband and at the mucocutaneous openings. If cases of lues are auscultated during the first few months of the disease, particularly after severe exertion, it is surprising to find how many of them exhibit cardiac murmurs. Those who receive adequate treatment seldom present such murmurs during the active stage of the disease, and doubtless, with the newer methods of treatment and better general knowledge of the disease among the profession, aortic valve disease will be less common in the next cycle. Usually those who had not been adequately treated do not complain of symptoms until about fifteen years after the appearance of the initial lesion.

Hard work and *alcohol* are common causes of arteriosclerosis in middle-aged men, and as such they represent fully a third of the remaining cases of aortic regurgitation. This form of the disease usually progresses very slowly.

The remainder of the cases, with a few exceptions mentioned below, are due to *infection.* Of these infections rheumatic endocarditis is the most frequent. The rheumatic fever of childhood is the condition in which the aortic valves are usually affected. Such involvement is rare in the rheumatic fever of adult life. When rheumatic fever is a cause the mitral valves are also commonly involved. These double lesion cases are of special interest, inasmuch as later in life a malignant endocarditis following infection is much more likely to occur than in those in which there is only a single lesion. Gonorrhea attacks the aortic in preference to the mitral valve, but it is a rare cause.

The few cases which are due to (1) traumatic rupture of the aortic cusps, (2) dilatation of an aneurysm of the ascending portion of the arch, and (3) congenital malformation are sufficiently rare to be regarded as pathological curiosities.

Symptomatology.—It is not always possible to draw a sharp line separating the symptoms of the valvular lesions from one another, nor can a course be drawn which will fit all cases. However, the symptoms of aortic disease are more definite than those of other diseases; and even when other cardiac valve diseases are superimposed the aortic syndrome dominates the picture.

A patient suffering from aortic disease may, and usually does, live for many years, suffering from time to time from what he considers to be minor symptoms. These are so slight that he rarely consults a physician, and close questioning will nearly always show that such symptoms have been present for five or ten years before a really severe break in compensation occurs. The earliest symptoms are those of cerebral anemia. This is due to disturbances of a mechanical character because of the circulatory changes resulting from the valve defect itself, and also from the coincident arterial changes in the brain itself. The earliest of these are loss of memory, roaring and thumping in the ears, relieved slightly by inflation, spots before the eyes, disturbances in sleep, and nose-bleed. Insomnia usually occurs in spells, and distressing dreams are frequent. Vertigo and partial fainting spells occur when the patient suddenly stands up or lies down. From time to time headaches are of frequent occurrence; they are usually temporal, and occur especially after exertion. Fits of mental depression and exhilaration are the rule. These are all thought to be due to nervousness; in fact, in this disease, more than in any other form of heart lesion, there is a remarkable reaction to mental influences. The pulse-rate increases, and the caliber of the vessels often changes at the least news of a startling character. Digestive troubles occur, but they are not characteristic. The facial appearance is that of a grayish-white anemia. The florid type is very rare.

The symptoms which lead the patients to consult the physician are usually pain and dyspnea. The pain is variously described. In many cases there is only a sense of oppression or fullness over the precordium. In others a sense of constriction or of weight in the chest is noted. In most cases, however, the pain is sharp and sudden and follows exertion or after a heavy meal. Most commonly it radiates down the left arm, usually along the inner surface, first to the elbow and later down to the little finger. Occasionally it involves both arms. These pains occur, of course, in aortitis and in other myocardial diseases, but they are more often associated with aortic than with mitral disease. After the pain has passed off there is usually a sense of numbness or recollection of pain, noticeable for some hours. Once the symptoms of secondary mitral insufficiency appear pain is seldom an outstanding symptom.

The dyspnea is of gradual onset, except, occasionally, when it occurs following severe exertion. It represents a functional insufficiency of the mitral valve. After a longer or shorter period the attacks of shortness of breath wake the patient out of his sleep. At first he can usually fall asleep again. After a time restlessness supervenes after the attack, and sound sleep is impossible for the rest of the night. Later on, Cheyne-Stokes breathing is quite frequently present. When this is noted the outlook is ominous.

Attacks of acute suffocative pulmonary edema are more common than in any other form of valvular disease, and they are usually associated with sclerosis of the aorta. These attacks come on suddenly, last for half an hour or more, and then disappear. The patient looks frightfully ill, but death during the attack is exceptional. Coughing and lung involvement do not commonly appear until mitral insufficiency takes place. During each break in compensation a fever of from 37.77° to 38.33° C. (99.99° to 100.99° F.) may be present, due either to a complication or to a recurring endocarditis. The presence of stenosis with regurgitation augurs better than either condition alone, inasmuch as when failure in compensation occurs it is more gradual and resembles the failure in mitral disease rather than that of aortic disease. Whether this is due to a lessening of the reflux of blood or to the fact that the patient feels that he must live a quieter life is open to question. Certainly the prognosis is better in the case of patients who present a double aortic lesion with symptoms than in those suffering from aortic regurgitation alone and accompanied by the same group of symptoms. Once the presence of either well-marked, frequent attacks of stenocardia, or of dyspnea on slight exertion occurs, the prognosis grows steadily worse. Soon there is further dilatation of the ventricle and relative insufficiency of the mitral valve, and the symptoms of mitral disease are added to the clinical picture. From now on the symptoms are those of broken compensation in general. Fits of melancholy and depression are the rule at this stage.

Even early in the disease an anxious expression may frequently be noticed in patients suffering from heart disease, and is spoken of as the cardiac facies. There is usually an anxious, staring look in the eyes, and tenseness of the mouth, and in the aortic cases there is a distinct widening of the palpebral slits. This closely resembles the facies of exophthalmic goiter. Sooner or later most patients with cardiac involvement who are bed-ridden show some mental aberration. At first it is only momentary—a single bizarre or uncalled-for sentence, or the patient becomes confused, and rights himself almost at once. Later these lapses become more marked. In some instances these mental changes last for several weeks or even months, but they are usually not continuous. During the day the patient is commonly quite calm; it is in the evening that most of this wandering occurs. When delirium is present it is seldom noisy. The patient almost always recovers himself when his attention is called to his lapses. He does not become maniacal or boisterous—the delirium is for the most part an endeavor to get away from his surroundings.

In aortic disease these pronounced mental symptoms often come and go for six months or more before death. In mitral disease, however, once this mental attitude appears it is seldom that the patient recovers from it, even temporarily. When it is marked and persistent it is an indication of approaching death, which usually ensues in a week or two.

Henry Head has described a special form of hallucination most common in aortic disease. The patient thinks that he sees a vision at the foot of his bed. This usually takes one of two forms, either that of a veiled female figure clothed in a light gray garment, and standing near the foot of the bed, or that of a man dressed to resemble the traditional undertaker, clothed in a long frock coat, with a large, white forehead.

These hallucinations usually occur about dusk or early in the morning. That these figures do appear will be readily admitted by any one who has judiciously questioned patients with serious cardiac involvement. Their significance, however, is not so clear. They form the basis of the layman's axioms as to the approach of death; after seeing such a figure the patient often foretells the approach of the end—sometimes correctly and sometimes otherwise. Whether it is the long illness of the patient and his consequent fear of approaching death which causes him to conjure up such specters, or whether indistinct images of objects seen are not clearly pictured on the retina because of the disturbed circulation, is an open question. The visions frequently disappear on the onset of mitral symptoms.

Aortic disease in children usually takes the form of a combination of organic mitral regurgitation with aortic regurgitation. In some instances the mitral lesion predominates, in others, the aortic. In those wherein the aortic lesion predominates the early symptoms are pallor, nose-bleed, cardiac pain and nervousness. In those in which the mitral lesion is most marked, dyspnea occurring early and later dropsy are the main symptoms.

In adults, in the form due to arteriosclerosis, the onset is insidious, with vertigo, insomnia and cardiac pain as the outstanding features. The pain is more marked than in the rheumatic cases. The mitral valve is not as frequently involved coincidentally as it is when the disease is due to infection. The accompanying dilated arch of the aorta is more common in the arteriosclerotic cases than in the rheumatic cases.

PHYSICAL FINDINGS.—*Observation.*—One can sometimes make a snap diagnosis of aortic regurgitation on inspection, but this is the exception. It is only when the carotids throb with each pulsation and the peripheral arteries pulsate that this is at all possible. The presence of the capillary pulse is of even greater value. This capillary pulse can be seen under the finger-nails immediately after they have been pressed upon and released. It appears as an alternate reddening and blanching under the point of pressure, or it may be demonstrated by drawing a pencil across the forehead and then observing the alternate waves of red and white following its trail. It is not very usual to find it well marked. It may be stated in passing that this capillary pulse is occasionally seen in patients who have a very low blood-pressure from any cause. Here again, however, it is uncommon. One may sometimes see the arteries on the temple straighten out and pulsate. As has been shown by McKenzie this straightening out and movement to the side is due to the fact that these vessels, because of the sclerosis, are crooked and much more elongated than normally. The powerful thrust of the column of blood tends to straighten them out, and gives the impression that they move from side to side with each beat. In well-marked cases of aortic regurgitation the eyes are wide open and bulge, suggesting the onset of Graves' disease. They are bright and moist. The complexion is pale gray or sallow. When the disease is established the apex-beat is displaced downward and outward, being almost always in the sixth space or below. Usually the farther down the apex is the greater is the hypertrophy, and the farther out it is the greater the dilatation.

If the patient is under forty years, and if the disease has lasted for some time, the chest-wall over the heart bulges more than it does in the right side. Of course, when the disease begins late in life this does not often happen. Except in marked decompensation the impulse is strong and regular. The reason for the heaving impulse is that in these cases of large hearts the apex is made up entirely of hypertrophied left ventricle. When the impulse is heaving and strong, hypertrophy dominates, whereas when the impulse is diffuse and feeble dilatation is in the ascendancy. Occasionally in the case of those suffering from severe anemia or from cachexia or loss of flesh, there are marked pulsations over the base and aorta, closely simulating those of aneurysm. This is especially the case if there is marked pulsation in the episternal notch.

Palpation.—Systolic thrills over the base of the heart are frequent. The arteries feel hard, large and thickened. When one palpates the radial artery, the pulse comes up against the finger suddenly and powerfully, yet it immediately falls away, and the vessel is apparently completely emptied. The large heart has expelled a great amount of blood into the aorta, and a part of this immediately falls back into the ventricle, leaving nothing to keep up the tension in the arterial tree. This is the cause of water-hammer or Corrigan pulse. If the arm is raised this phenomenon can be more readily demonstrated to the student.

The researches of Hewlett and Van Zwalenberg have shown that much of this collapse of the pulse is due to a reflux of the blood from the peripheral arteries into the aorta. On the other hand, the absence of the collapsing pulse in aortic regurgitation does not necessarily indicate the presence of aortic stenosis, inasmuch as this type of pulse may not be present unless there is considerable reflux. The pulse is always retarded or delayed. There is a much longer interval of time between the beat of the heart and the radial pulsation than in normal patients. This varies according to the amount of regurgitation present. This delay is most noticeable when the hand is raised above the head. The Corrigan pulse is present in most of the rheumatic cases. When lues is the cause, the proportion of distinct Corrigans is decidedly less.

Percussion.—The area of percussion dulness is increased to the left and often reaches the anterior axillary line. The upper border may reach the third rib on the left side. There is usually a slight dulness to the right of the sternum, near the base.

Auscultation.—A diastolic murmur at the base of the heart is the most reliable and constant auscultatory evidence of aortic regurgitation. This is due to a return of the blood from the aorta through the partially closed valves, after the systole of the ventricle has thrown it into the vessel, and while the ventricle is once more being filled by the blood from the auricle. The quality of the murmur depends upon the size and character of the opening and upon the pressure in the vessel itself. For that reason a small leak associated with sclerotic valves with a high pressure may cause a much more intense murmur than if a large amount of blood is thrown back through the large orifice. In any case a calcified orifice causes a louder murmur than a flexible one, which may yet be the site of a very much further advanced lesion. The murmur is of greatest intensity in one of three places:

(1) On the chest surface, at a point over the valve just as the junction of the sternum with the left third costal cartilage. Occasionally this is not the case, inasmuch as the conus arteriosus of the pulmonary artery is here placed between the aorta and the chest-wall and because its large size may interfere with the transmission of the sounds.

(2) On the right side of the sternum at the junction of the second costal cartilage.

(3) At the fourth left intercostal space at the edge of the sternum.

A frequent cause of this variance in intensity depends upon which cusp of the valve is most markedly affected. Each cusp vibrates differently, and thus transmits sounds of different intensity. The different points at which the murmur may best be heard, together with its transmission, as well as the ultimate cause in most instances, may be fixed in the minds of the observer in the following manner: An ink mark is placed over each of the points above mentioned, also over a point in the neck at which the murmur is clearly heard. If these four points are connected by outside lines, an irregular parallelogram is formed, which somewhat resembles a crude diagram of a vagina—the ultimate cause of the lesion.

In rare instances this murmur, like the murmur of aortic stenosis, is best heard just outside the hypertrophied apex in the anterior axillary line. Often it is not widely transmitted, and yet when it is very loud it can be heard all over the chest-wall. Sometimes the high-pitched faint murmurs are best heard by placing the ear against the naked chest-wall.

This murmur is, however, often overlooked, due to the fact that it is frequently so soft. It is either a blowing or a purring sound. It can sometimes be brought out by exertion; in other instances exercise makes it inaudible. Like all murmurs it may be present at one examination and missing at the next, so that one positive finding is worth a dozen negative ones. The character of the murmur varies. In the case in which it is frequently missed it is only a mere whiff after the second sound. In other instances it is quite raucous. It is heard well down along the sternum as far as the fifth costosternal junction. In many of the cases due to arteriosclerosis it is not transmitted into the vessels of the neck. Having the patient sit up and bend forward often serves to bring out the murmur. An aortic systolic murmur is present in approximately one-half of these cases. Sometimes one hears this systolic murmur at the base, in the course of aortic regurgitation, and yet on postmortem examination no stenotic or sclerotic changes are found. This has been explained as being due to the fact that at the beginning of ventricular systole the regurgitant flow has not entirely ceased, and when this latter flow meets the opposing current a murmur is produced which is systolic in time. When aortic regurgitation occurs in children it is quite common to find also a systolic murmur present at the apex, due to a coincident mitral regurgitation. The first sound of the heart is loud and long, due to the great quantity of blood which is thrown out in systole. The murmur is usually present at the end of the second sound. Sometimes, however, it occupies the entire diastole.

According to Broadbent, the long, loud diastolic murmur shows that considerable pressure is kept up by the aorta; it is a sign that hypertrophy is present, and that the leakage is not very great. On the other hand, a weak, short murmur shows that the heart is weak, and is, therefore, a bad sign. When dilatation occurs the first sound at the apex is superseded by a systolic murmur, which is due to a relative mitral insufficiency. When dilatation has been overcome this murmur disappears and a clear first sound reappears.

In about one-third of the cases the first sound at the apex is vigorous and somewhat resembles the slapping sound present in mitral stenosis. The protodiastolic gallop rhythm is frequently heard in aortic regurgitation, especially when there are evidences of broken compensation.

Flint Murmur.—Austin Flint described a murmur that is frequently present in aortic regurgitation, and is identical in time and character with that of mitral stenosis, and can scarcely be differentiated from it. Flint believed it to be due to a functional mitral stenosis, and this theory has thus far not been seriously controverted. It is more commonly found when the aortic regurgitation is due to rheumatic fever than when lues is the cause. It is more fully discussed under mitral stenosis.

Evidences of Aortic Regurgitation Outside the Heart.—Frequently a coincident stenosis is present, or at least there is a roughening of the aortic valves, causing an aortic systolic murmur, which is transmitted up to the vessels of the neck. In the larger arteries a to and fro murmur is frequently present. It is best heard over the femoral artery and is known as the murmur of Duroziez. This phenomena is believed to be due to low diastolic pressure. When the stethoscope is placed over the femoral artery, and pressure exerted, a sharp systolic sound (pistol shot) is sometimes heard. This is a local phenomenon and may be heard to a lesser degree in many other conditions.

Special Examinations. — *Sphygmograph.* — The sphygmographic tracing is characteristic. The up-stroke is high and almost perpendicular, and forms a very acute angle with the sharply descending down-stroke.

From a diagnostic standpoint exact measurement shows that the diastolic notch in the collapsing pulse falls below the middle of the pulse-wave, while in the normal and anacrotic pulse it lies above the middle of the wave (Hirshfielder): To put this in other words, in the Corrigan pulse over one-half of the fall of pressure occurs during systole, while in normal pulse the fall occurs chiefly during diastole.

Blood-pressure.—The blood-pressure is regularly high in the patient presenting symptoms; it is rare to find it below 160 Hg. The pulse-pressure is usually about 100. In fact, when one takes a blood-pressure measurement by the auscultatory method a tapping sound is often heard until the mercury goes down to zero, so that the diastolic reading must be taken by the oscillating method. When the patient is in a recumbent posture, the blood-pressure in the leg is from 50 to 100 mm. higher than it is in the arm, and this fact has considerable diagnostic value.

Electrocardiograph.—The evidence of left-sided hypertrophy is an extremely prominent S-wave in lead 3, whereas the R-wave in lead 1 becomes larger than the R-wave in lead 2.

X-ray.—The outline in aortic valve diseases is more constant than it is in mitral lesions. The region about the apex is enlarged and obtuse. The apex itself is out near the axillary line. The body of the left ventricle is egg-shaped. This is called the duck-heart, because of its resemblance to a sitting duck.

Fluoroscope.—One of the usual accompaniments is the aortic fling, *i.e.*, the underexcursion of the aorta during beats, which is a very striking phenomenon. In severe cases it closely resembles the picture of aneurysm and is commonly diagnosticated as such when read from a single *x*-ray plate. There is also a sharp left ventricular contraction with a distinct lifting motion about the region of the apex. In uncompensated cases this movement appears to be separated from the rest of the ventricle.

Diagnosis.—The diagnosis of aortic regurgitation is commonly not difficult. However, there are five conditions which may occasionally cause trouble: (1) the murmur of mitral stenosis; (2) the Flint murmur; (3) the Graham-Steele murmur; (4) pulmonary insufficiency (see Diagnosis under Mitral Stenosis); and (5) aneurysm.

Of these only mitral stenosis causes any great difficulty. This becomes particularly noticeable when the murmur of mitral stenosis is diastolic in time rather than presystolic. The Flint murmur, when occurring at the same time, may be a disturbing factor, especially when it is loud and the aortic murmur is soft and indistinct. A third, confusing murmur is the so-called Graham-Steele murmur which accompanies the murmur of mitral stenosis. It is heard best along the left sternal border and is not transmitted down to the apex.

When one of these three murmurs is present and its limitations are not strictly defined, we are most likely to establish the diagnosis on the basis of the peripheral signs, such as: Corrigan pulse; blood-pressure changes in arm and leg; pistol-shot sound; Duroziez murmur; and a history of rheumatic fever or of syphilis.

Differential Diagnosis.—In the presence of a well-marked throbbing of the vessels of the neck, with few other characteristic signs, the question of the presence of *aneurysm* is frequently raised. Many of the symptoms are the same in both diseases, *i.e.*, the pain in the chest, the cardiac hypertrophy and the history of lues are similar in both. In aneurysm there is usually a systolic murmur, but often there are both systolic and diastolic murmurs. In these doubtful cases, in which there is no characteristic aneurysmal bruit, the most distinctive auscultatory sign is a sharply accentuated clanging, second aortic sound. The more plainly this sound may be heard away from the second right costal cartilage, the greater becomes its diagnostic import, as proving the presence of aneurysm. Of course, in the presence of other characteristic signs, such as tracheal tug, marked dulness at the base, inequalities of the pulse, thrill, etc., there is little trouble in arriving at a conclusion. The frequency with which the two lesions are coincident must always be kept in mind, and in every case of aortic regurgitation one should consider the possibility of a concomitant aneurysm. However, aneurysm is more commonly complicated by aortic regurgitation than *vice versa*. Finally, in all cases in which there is any doubt either as to diagnosis or as to the presence of both lesions fluoroscopy is the court of last resort.

Some clinicians describe a functional aortic regurgitation due to dilatation of the mouth of the aorta, or occurring as an accompaniment of *pulmonary insufficiency*. Among the rarer disturbing conditions, from a diagnostic standpoint, is *severe pernicious anemia*, which produces murmurs at all orifices; these are especially marked over the great vessels and sometimes produce a pseudo-collapsing pulse. Another rare diastolic murmur is sometimes heard over old pericardial adhesions.

Mediastinitis, because of adhesions about the vessels, produces a cardiorespiratory murmur which may be confusing. It is loudest during inspiration and often disappears with change of posture.

Rupture of the valves is recognized by the sudden onset of symptoms after severe exertion. There is pain, a tumultuous action of the heart, and a loud diastolic murmur.

Treatment.—This is the disease of the heart above all others wherein **careful living** and avoidance of extremes are of most importance. Nowhere else in cardiology is the regret of "what might have been" more properly applied, because a single rash act may precipitate a fatality, whereas with care the same individual might have lived many years. These accidents are most apt to happen shortly after the inception of the lesion, before the heart has enlarged sufficiently to overcome the likelihood of sudden dilatation. This, of course, obtains only for those cases which occur following the infections, particularly rheumatic fever. When it follows syphilis or arteriosclerosis the onset is so slow and so insidious that little good can be accomplished by rest in bed for a prolonged period.

The patient who suffers from aortic disease must be especially **warned against a sudden exertion of any kind,** because of the possibility of sudden death. It is,of course,needless to say that one should not warn such a patient of the likelihood of sudden death. However, his friends should be warned of the possibility, and it should be impressed upon the patient himself that every such act will render his condition irretrievably worse. Oddly enough such patients do not usually die at the time of the excitement, but during the hours and days following. These aortic patients are particularly apt to have very positive views and are with difficulty restrained. Such patients should take vacation every few months, and during this time should remain in bed for three or four days.

If at any time there is a change in the character of the pulse or extension outward of the apex-beat, **absolute rest** must be enjoined for a month at least.

When these aortic cases present such urgent symptoms as severe pain and dyspnea, sudden death is at any time a probability.

If one divides the causes of aortic disease into rheumatic fever, arteriosclerosis and syphilis, it will be seen that there is little hope of permanent cure or satisfactory medication except in the last group. And even here miracles cannot be performed.

There are no specifics for the rheumatic group, although **salicylate** will occasionally relieve pain and some of the minor symptoms.

In the arteriosclerotic group the use of **potassium iodid** is of undoubted service both in lessening the progress of the disease and in alleviating the symptoms. In those cases which are due to syphilis, repeated courses of small doses of **salvarsan** are indicated. Certainly every such patient should have one or more courses every year at least. In the absence of this, one must resort to yearly courses of **mercury** or potassium iodid, even if there are no symptoms whatsoever. The presence of active symptoms, naturally, calls for more frequent use of these agencies. One can never imagine a luetic lesion of the valve as being stationary. When symptoms occur, such as pain and dyspnea, potassium iodid is of value in itself in relieving the symptoms. **Digitalis is not indicated** in aortic disease unless there are evidences of broken compensation. For the relief of the symptoms—and these are usually of a nervous character—sedatives for the nervous system are indicated; **bromids** in 20 or 30 grain (1.3 to 1.95 gram) doses three times a day are efficacious for the relief of the milder symptoms. When sleeplessness and palpitation are marked, one must often resort to **chloral** or some other hypnotic. **Morphin,** however, is the sovereign remedy, and does more to prolong the lives of these patients than any other single medicament. They must have sleep, and a hypodermic of morphin is the best means of producing this result. Sometimes small doses of morphin and chloral by mouth act better than a large dose of either.

When the evidences of mitral failure are apparent, such as edema, enlarged liver, etc., then the case must be treated along the lines of mitral disease, with this exception, that as soon as compensation begins to improve, the dose of digitalis must be reduced.

Prognosis.—The outlook depends upon (1) the cause of the lesion, (2) the stage at which it is discovered, (3) the extent of the circulatory changes outside of the heart, and (4) the extent of involvement of the other valves.

In adults, if the lesion is due to a rheumatic endocarditis, the outlook is favorable. It is not very much worse than that for uncomplicated mitral disease, provided the blood-pressure is low and the apex is within the nipple line. After an acute attack of rheumatic aortic endocarditis, it is no rarity to find a well-marked Corrigan pulse, a pulsating aorta, and hypertrophy with no distinctive symptoms, and yet these patients may live for decades in apparently good health.

In the case of a patient under twelve years of age, the outlook is not favorable because of the likelihood of the development of a fresh attack of endocarditis. Especially is this true when, as is so often the case, there has been a coincident involvement of both mitral and aortic valves. Here the added likelihood of the development of malignant endocarditis at a later period should always be kept in mind. When the disease is the result of atheroma the eventual outlook is worse than when it is due to any other cause, because the lesion is always a progressive one. This progression may, however, be a matter of many years, and the prognosis must be based upon the length of time it has existed when discovered. If the disease is relatively early there is little immediate danger, and serious events may not occur for five or ten years. The progressiveness of this basic lesion rather than the involvement of the valve itself is particularly dangerous. It almost always involves the coronary vessels and their orifices, and is thus responsible for more of the anginal attacks and sudden fatalities than is the valvular lesion itself. This stenosis frequently involves the kidneys also, and not infrequently kills through these organs rather than through the heart itself. This type is associated with sudden death more often than with the case due either to rheumatism or syphilis. It is a particularly serious form of the disease in young people, inasmuch as here the progress is more rapid than in the aged. This progressive arteriosclerotic process in young people is sometimes a family trait, and when this is the case, other things being equal, the age of death will be approximately the same as that of the ancestor. The most frequent cause of aortic regurgitation is syphilis, and here the outlook depends upon the adequacy of treatment, the time of discovery of the lesion, and the time of the appearance of symptoms. In approximately one-half of the cases of syphilis there is some involvement of the heart, yet it is frequently not made evident by the appearance of any physical sign. These changes usually take place in the acute stage, and the results are not noticeable until years after. The lesion is generally discovered only on examination for some symptoms of cardiac failure. In the ordinary hospital case this is, on an average, fifteen years after the appearance of the initial lesion. Such patients, as a rule, only take treatment until the disappearance of the secondary symptoms, or, on an average, about three months. Occasionally the lesion is discovered during an examination for life insurance in one who is free from symptoms, and here treatment materially improves the prognosis. Yet even here twenty years seldom pass between the appearance of the lesion and cardiac failure. In the case of patients who present themselves for the first time after symptoms have appeared, life is seldom prolonged more than three years, in spite of treatment. Usually death occurs in less than one year if the presenting symptoms are very marked. Unquestionably treatment alleviates some of the symptoms, particularly the anginoid pains, but it seldom produces the marvelous results which are obtained elsewhere in the body by specific medication. Once the murmur of organic aortic regurgitation is present it never permanently disappears. In general a long, loud murmur is better than a short, faint murmur. A harsh second aortic sound heard in the vessels of the neck independently of the murmur shows that the leakage is slight and that the outlook is good. The presence of the Flint murmur does not materially affect the immediate prognosis, although it shows that the disease is relatively far advanced. The more collapsing the character of the pulse the greater the regurgitation, and, with the exception of the cases which are due to rheumatic fever, the worse the prognosis. On the other hand, without this collapsing pulse the presence of uncomplicated aortic regurgitation is not very grave. When combined with aortic stenosis the absence of the collapsing pulse is not necessarily hopeful. When a well-marked collapsing pulse has once been present and then disappears the outlook is bad. When the blood-pressure, either systolic or diastolic, is not markedly raised, and the pulse is normal in frequency, the outlook is good. If the blood-pressure is elevated, but does not steadily rise, the outlook is favorable for the time being. A marked fall in blood-pressure is ominous. When the pulse becomes permanently rapid without any appreciable cause the eventual outlook is serious. When it remains at 90 or above and does not react to ordinary measures and to digitalis, the progress is generally intermittently downward. Not infrequently we find the pulse quite good continuously up to the minute of death, or even better than it has been for weeks previously, but usually this is not so, and it is decidedly weaker, even though it is regular on the last day or two of life. When the patient presents himself, some of the symptoms of added mitral disease are generally present, and the more marked the evidences of mitral decompensation the worse the outlook. In aortic disease, except the form due to rheumatic fever, the patient seldom recovers temporarily from more than three breaks in compensation, whereas in primary mitral disease recovery may follow many attacks which threaten life. Once pulmonary stasis occurs the patient seldom recovers. Attacks of severe dyspnea in aortic disease are of much greater consequence than in mitral disease, because they mean at best a functional mitral regurgitation which is equivalent to a weakness in the ventricular wall. Such attacks are frequently the beginning of the end. When auricular fibrillation occurs in aortic disease, unless aortic disease is due to a rheumatic infection, it does not react to digitalis, and the progress of the disease is steadily downward. As in all forms of cardiac disease the outlook is better for women than for men. Sometimes, when aortic regurgitation is met with in youth, and is quite severe and progressive, and an early fatal termination seems inevitable, the disease will apparently cease its progression on the addition of the murmur of aortic stenosis producing the seesaw murmur, and the patient may live for years. Most of the sufferers from aortic disease die as the result of an intercurrent disease, and the majority are associated with a functional mitral regurgitation during the terminal infection. Many die of one of the sequelæ of syphilis or of arteriosclerosis in other parts of the body. Attacks of anginoid pains, rapid weakening of the heart-sounds, with a pericardial friction rub at the base, are not uncommon, and usually indicate death within a few days. Mental aberration is particularly common toward the end of the progress of aortic regurgitation. An extra systole, not previously present and not due to digitalis medication, is sometimes a harbinger of the end. Angina pectoris and acute suffocative pulmonary edema are frequent terminal events. Death in angina pectoris usually occurs at the beginning of the attack rather than at the end. Death is not so common in the severe and prolonged attacks of angina pectoris, but the patient often dies a day or two after the attack. In such cases the frequency of the heart increases, pressure falls, and pulmonary edema follows. The angina apparently acts as a sort of reflex inhibition on an already damaged organ. As a rule patients suffering from aortic regurgitation are in and out of bed until the last few weeks of life, and death is unexpected. Sudden death is more common in patients suffering from this than from any other valvular lesion. The atheromatous patients are particularly apt to die in this manner. On the other hand, the rheumatic cases seldom die suddenly. Sometimes death occurs during sleep; commonly, however, it follows after or during some strenuous exertion. It happens most commonly in those who have not complained of any decided symptoms and who consider themselves quite well. It occurs not infrequently during sexual intercourse. Thus, each year, the city papers record the fall of some country church pillar who has died in the arms of an urban Delilah.

Pathology and Pathological Physiology.—The pathology varies somewhat with the cause. In the cases due to syphilis there is an arteritis of the fine vessels at the base of the valve. This produces degenerative changes that are to be seen as plaques, the size of a pinhead and larger. Their color varies from pink to gray and yellow. They consist microscopically of an infiltration of the subendothelial tissue with layers of round- and spindle-cells. In these cases this process is not confined to the valve alone but is apt to involve the openings of the coronary orifices, finally occluding them, and often extending down the vessel itself. This probably is the reason for the frequency of angina pectoris in syphilitic cases. In other cases the scar tissue produced by the lesion in the valve contracts and produces varying deformities. This is most commonly the result in those cases which are due to infection. The edges are curled back or become adherent, calcification takes place so that the valve can not come into apposition during diastole, and a leak results. The amount of leakage depends upon the degree of this faulty apposition and upon the tonus of the cardiac muscle, which attempts to overcome the leakage. Because of this irregularity and rigidity of the segments there is of course also some stenosis. In the arteriosclerotic cases there is a gradual thickening of the cusps which become hardened and retracted. In these cases also there is often, but by no means always, a general involvement of the arch of the aorta and of the coronary orifice. Here again this is a frequent cause of the painful anginal attacks. The cases due to endocarditis usually occur in youth, there is no involvement of the aorta itself, nor of the coronary orifice, and the disease is not progressive unless there is a fresh attack of endocarditis. As a consequence of the back pressure which is gradually produced, the heart becomes able to adapt itself to the greater amount of work and consequently hypertrophy results. This produces the greatest enlargement of the heart that is ever met with. It is frequently called the beef heart because of its resemblance in size to that of a cow. The researches of Stewart have shown that there is also another factor in the production of this hypertrophy. As is well known, unstriped muscle always reacts to a stimulus. In the heart it is ordinarily the stimulus which follows the distention of the ventricle resulting during diastole. In regurgitation there is some distention almost immediately after systole, so that the tone of the muscle of the ventricle is almost constant throughout nearly the entire cardiac cycle, and consequently an hypertrophy of the muscle is developed. In the latter stages, either because of greater reflux or because of degeneration of the hypertrophied muscle, the ventricle gradually enlarges and thus separates the base of the mitral valves, causing a space to exist between their free edges. A relative mitral insufficiency is the result. Of course, after this occurrence all of the phenomena of broken compensation are in evidence. The extra effort of the ventricle to expel the blood which flows in during the diastole from the mitral orifice and that which is regurgitated from the aorta causes a high systolic pressure in the arteries. The instantaneous regurgitation of the blood after its expulsion accounts for the sudden drop of the column of blood, and this produces a low diastolic pressure; consequently the pulse-pressure, *i.e.*, the difference between systolic and diastolic pressure, is very high. When these alternate high and low pressures are kept up for a long time, a general arteriosclerotic change takes place.

MITRAL REGURGITATION

Etiology.—This is by far the most common valvular lesion met with in practice. The mitral regurgitant murmur constitutes 50 per cent. of all of the simple, uncomplicated organic murmurs heard. If combined lesions are counted, it is present in more than two-thirds of all the patients suffering from chronic endocarditis.

The distinction between organic and relative, or functional incompetence, must be made more commonly in this disorder than in mitral stenosis. In fact, diastolic murmurs are rarely functional, whereas systolic murmurs are frequently due to functional or relative incompetence, or are accidental.

The mitral organic murmur is in most instances due to a previous chronic endocarditis. Certainly in patients under twelve years of age, if fetal abnormalities and chorea can be excluded, all cases of endocarditis may be considered as due to rheumatic fever. In these patients the presence of two large central incisor teeth in the upper jaw are strikingly suggestive. They are called tombstones. People who have these prominent teeth appear to be more likely to contract the rheumatic infection than are others. In a child the term "tombstones" for such teeth is quite appropriate; it suggests the sequelæ; *i. e.*, rheumatic fever, endocarditis, death, and tombstone.

Mitral disease is synonymous with rheumatic fever in adult life, up to forty years of age. The exceptions to this rule are extremely few. When the onset is after fifty years of age a large proportion of cases are due to arteriosclerosis; very exceptionally does one meet with incompetence due to trauma such as follows rupture of the chordæ tendineæ from exertion.

Relative incompetence is quite common. It is accountable for the murmur sometimes met with immediately after severe exertion or during severe infection and wasting disease, tuberculosis, chronic nephritis, myocarditis, and in the course of aortic regurgitation. The distention of the chambers of the heart separates the bases of the valves, and this must necessarily separate the edges of the valves, thus allowing some regurgitation.

On postmortem examination the evidence of such a relative incompetence can seldom be demonstrated. Roughly speaking, about one-half of such murmurs disappear after a short interval.

Symptomatology.—GENERAL SYMPTOMS.—While it is true that each form of chronic valvular disease presents some symptoms which are peculiar to itself, practically all forms sooner or later present the mitral regurgitant and tricuspid syndrome in their terminal stage. The early distinctive symptoms of mitral regurgitation which are commonly linked up into those of mitral stenosis have to deal with stasis in the pulmonary circuit, and are (1) cough, (2) dyspnea, and (3) other respiratory disorders, such as hemoptysis, all of which are primarily due to left heart-failure, whereas the later symptoms of this lesion, as well as of all forms of chronic valvular disease, as (1) cyanosis, (2) enlargement of the liver, and (3) a gradually ascending edema, are due to right heart-failure. Most patients suffering from mitral regurgitation experience a number of minor complaints for a long time before consulting a physician. These are due to various minor circulatory changes, often of a transient nature, the pathology of which is not always clear. Weakness is the earliest of these symptoms to appear. Its onset is usually so gradual that the patient is afraid of being accused of laziness, and this he feels keenly. In other patients it is only noticed after severe exertion. This weakness must not be confused with the nervous trembling and dyspnea which, in normal people, follows unusual exertion. The sense of inability to do work of any kind, whether it is mental or physical, often appears to an onlooker to be a mental as well as a physical fatigue. The patient's commonest complaint is that he cannot drag one leg after another, especially at the end of the day. Another form of the same symptom is a feeling of fatigue in the throat at the end of the day. The patient feels as though he had talked too much. In fact, all cardiac symptoms are end-of-the-day symptoms. Of course this sense of weakness and fatigue is not pathognomonic of cardiac disease, for it is met with in many other disease conditions; but when it occurs for the first time in a middle-aged person it is always a suggestive symptom.

Another evidence of such congestion is the slight cardiac cough. It is apparent during exertion when climbing a hill, going out into the cold or beginning a conversation. It is different from an ordinary catarrhal cough in that as a rule it is not repeated. The patient is usually not conscious of this. Increased sensitiveness to cold is not a frequent complaint. However, nearly all patients with cardiac involvement feel worse in cold weather. Palpitation and a sense of powerful heart-beat are sometimes complained of, but this is a complaint more commonly present in those who are free from heart disease.

An early result of circulatory disturbance in mitral regurgitation is stasis in the capillaries of the lung, and this is the ultimate cause of dyspnea. For that reason shortness of breath is the earliest subjective evidence of mitral regurgitation. This stasis does not occur provided the left ventricle is strong enough to prevent it; for that reason it is not present in any case until there is some failure of the ventricle —either because the leak is too large or the ventricular muscle too weak to overcome it. When there is any severe strain, such as results from unusual exercise, it becomes apparent. This explains why many patients do not show the slightest evidence of dyspnea, even though the murmur is very pronounced. Every one has met with such cases in athletes or in very strong, vigorous people who, on being examined for other purposes, are found to have pronounced mitral disease which must have been in existence for years without producing the slightest symptom of any kind. These cases, however, must be regarded as the exception rather than the rule. After existing for a longer or shorter period the continued pressure in the capillaries of the lung causes changes in the vessel-walls and in the surrounding tissue which favor the production of a chronic bronchitis, thus still further increasing the dyspnea.

There are many patients who never show any other symptom than dyspnea until near the end. Those who present symptoms earliest are those who have had endocarditis in childhood. Relative insufficiency, such as that resulting from fever or anemia, seldom gives rise to any symptom except dyspnea on exertion and a sense of weakness. Inorganic heart disease, and later the attacks of dyspnea which formerly occurred on climbing a hill, going out in the cold, or facing a wind, or following any unusual exercise, and which quickly subsided, fail to stop so quickly, because the reserve power has been used to its utmost. These attacks now come on in the middle of the night while the patient is asleep, and their occurrence is not in any way casually related to physical exertion. Often there is associated with these attacks a desire to evacuate the bowels, also a belching, which the patient believes gives him relief.

Just why cardiac patients have these night attacks has never been satisfactorily explained, because it is not due, in the majority of instances, to dreaming, nor to indigestion. In the advanced cases in which dyspnea follows immediately after falling asleep the ultimate cause is a diminished sensitiveness of the respiratory centers which allows carbon dioxid to accumulate more readily than when the patient is awake.

The patient is first restless, then he breathes with very shallow inspirations, and finally forgets to breathe at all. Then he wakes up with a start and has a paroxysm of rapid breathing associated with terror, which makes him still worse. Often this happens just as he is falling asleep. Oppression on the chest during this paroxysm is the chief complaint. The recollection of such spells causes the patient to try to stay awake sooner than go through this terrible ordeal at night. The loss of sleep in its turn reacts badly on the sick one, aggravating his condition; finally the dyspnea occurs during the day on the least exertion.

When the disease has advanced to the point where the patient must sit up in bed in order that he may breathe without distress the condition is termed orthopnea. This orthopnea is characteristic of cardiac disease, and has some diagnostic value. In no other disease, with the possible exception of aneurysm, is it so necessary for the patient to sit up in order that he may breathe. One may occasionally make a diagnosis on entering a ward or the sick room, on the basis of this phenomenon. The least attempt on the part of the sufferer to lower his head is followed by a distressing dyspnea; in fact, his progress toward recovery may often be measured by the gradual diminution of the number of pillows necessary for his comfort. This orthopnea is often developed within a day of the onset of decompensation. It is perhaps the most serious of the major symptoms.

Susceptibility to attacks of bronchitis, particularly during the winter months, is the rule in mitral cardiac cases of long standing. These attacks last so long, and are so resistant to treatment, that the laity are often alarmed as to the likelihood of the onset of pulmonary tuberculosis. A loss of flesh, slight rise in temperature and cough with bloody expectoration form a picture which is indeed strongly suggestive of tuberculosis. When dyspnea becomes a marked symptom, other evidences of venous stasis due to right heart-failure usually appear. Sharp pain is uncommon in mitral regurgitation unless stenosis is also present; on the other hand, uncomfortable sensations about the heart, and tenderness of the skin over it, are frequently present. The patient and physician commonly ascribe these to the indigestion so often accompanying cardiac disease. The evidences of right heart (tricuspid) failure must be considered as part of the mitral regurgitation, inasmuch as they are almost always a direct sequence or concomitant of it. A slight cyanosis sometimes appears before there are any other signs, due to peripheral stasis, and produces a bluish tint of the cheeks and ears. If this lasts sufficiently long it is associated with the clubbed fingers which are always so suggestive of circulatory disease. The terminal phalanges appear as though they had been crushed back with a hammer, and usually are different from those due to pulmonary disease, which are enlarged but of an almond shape. These distinctions are not always definite and clear-cut, for pulmonary and circulatory diseases are often combined; but they frequently suggest that one or the other of the organs is the cause of the deformity.

The first symptom which really frightens the patient is edema. The word "dropsy" is associated in the mind of the layman with "Bright's disease and death." Unless it is absolutely necessary to warn the patient as to the seriousness of his condition, the term "dropsy" should not be used in his presence.

Edema of the legs is due to failure of the right heart and not of the left. In nearly all cases of cardiac failure it is present at some time or other, but it is preëminently a mitral symptom. The ultimate cause of this edema is a debatable question, but a large part of it is due to a local stasis, and it begins where circulation is most retarded. This is in the dependent portions of the body when the patient is up and about.

This slowing of the circulation is, of course, manifest at first only during the latter part of the day when the cardiac weakness becomes evident, disappearing after the night's rest and the equalization of the circulation. After the edema has disappeared in the morning, pressure over the former edematous region is exquisitely painful and is a sign of some value, showing that edema has been present. Later, as the weakness and leakage of the right auriculo-ventricular valve increases, it becomes continuous and gradually moves up the legs to the abdomen. This progression is quite different from the edema occurring in nephritis, where the edema is due to a toxin, and where it is quite as bad at one time as another and is generally universal. Even here, however, sooner or later the heart is involved, and the edema is worse in the dependent portions of the body.

When the edema has extended to the thigh, ascites is the rule. It is, however, not always demonstrable.

It is very rare, in mitral regurgitation, for ascites to precede edema of the legs, and in any case in which this happens one must look for other causes of the ascites. The same holds true with hydrothorax.

While ascites is a serious symptom, the patient often recovers from it entirely and may live for years thereafter. When ascites can be demonstrated, right-sided hydrothorax is generally also present. When fluid can be demonstrated reaching up to the angle of the scapula it should be removed, as it is a distinct menace to the patient. This hydrothorax affects the right side in preference to the left, because of the anatomical position of the major azygos vein which drains the intercostal spaces and pleura. The vein enters the superior vena cava at an oblique angle, and thus the least pressure of an enlarged right heart produces an obstruction. The hydrothorax increases the work of the heart by pressing on the right lung and by pushing the heart further to the left. Another explanation is that it is due to postural edema, the patient usually lying on the right side. It is an occasional cause of sudden death.

At about the same time that the edema is marked the liver becomes noticeably enlarged, and is the first *palpable* evidence of broken compensation, just as the presence of fine subcrepitant râles at the base of the left lung, when the patient sits up after having been on his back for some time, is the first definite *auscultatory* evidence of failing compensation. The liver is large, smooth, hard, and has rounded edges. It is often a hand's breadth below the margin of the ribs. Following the early breaks in compensation it almost always recedes and cannot then be palpated during the interval. This recession of the liver is a good omen. After repeated breaks in compensation it becomes permanently hard and enlarged. A slight icterus, not a well-marked jaundice, but rather a muddy complexion, is commonly also present. The whole clinical picture of icterus, enlarged liver, and dropsy, when seen for the first time, closely resembles a case of cirrhosis of the liver and is frequently so diagnosticated. A dull pain over the epigastrium is a very common complaint. This is due to cardiac dilatation and to enlargement of the liver, and is a comparatively late symptom. Digestive disturbances due to concomitant venous engorgement of the digestive tract are commonly present quite early; yet in many cases they do not appear until anasarca is quite general. Among these the earliest is belching and a sense of fullness after meals; later on there is anorexia, and, as the case progresses, vomiting is commonly present. Often this vomiting is mistakenly thought by the patient and physician to be due to medicine ingested. In some cases periodical diarrheas occur.

Kidneys.—About this time the urine is much diminished and presents all the signs of passive congestion, that is, a small amount of albumin and hyaline casts. Sometimes it is difficult in the first few days to differentiate such a urine picture from that of the concomitant nephritis.

Indeed, in all moderately advanced cases of cardiac disease, a trace of albumin, and hyaline casts, are commonly present in the urine at the end of the day.

Because of the extensive edema, it is often difficult, when the patient is first seen, to determine whether one is dealing with a primary cardiac lesion, with edema, due to passive congestion, or to a primary renal lesion with secondary cardiac changes, or to a combined cardiac and renal disease. It is uncommon to find large amounts of albumin for more than a day or so in patients with uncomplicated heart disease. Usually only a trace of albumin is present, no matter how severe the edema may be.

Granular casts are not common in the severe cases of passive congestion of the kidney secondary to cardiac disease, while they are the rule in kidney disease. In the presence of marked decompensation the pthalein test is of no help in making the differentiation from true renal disease. However, after a few days of rest and treatment the output approximates the normal in the cardiac cases, whereas there is little change in the nephritic cases.

In the cardiac cases, the sodium-chlorid excretion is only slightly interfered with, so that restriction of salt in the diet does not produce the marked results that it does in the edema of nephritis. In the primary cardiac cases, the blood-pressure is commonly low, whereas in the majority of renal cases it is high.

In many patients the minor symptoms, with perhaps a little shortness of breath on exertion, are all that are noticed for years. Every now and then, however, usually as the result of an acute infection or of some sudden severe exertion, the symptoms are exaggerated, and some of the more grave complaints are added, even threatening life itself. These complications are usually evident in the shape of a severe bronchitis, bronchopneumonia, or pulmonary edema. Under rest and treatment the attack is recovered from and the patient is apparently as well as before. Repeated similar attacks with minor symptoms during the interval constitute the life history of such patients, yet years may intervene between attacks. Finally some of the major symptoms persist during the interval, and then the progress is steadily downward.

PHYSICAL FINDINGS.—*Inspection.*—The mitral facies will be described under Mitral Stenosis. The precordium is prominent in children, and if the disease is of long standing, the same is true of adults. The area of the apex-beat is commonly enlarged; at a later period it becomes diffuse. It is a more extensive impulse than is present with any other cardiac lesion, not excluding aortic regurgitation. It is usually dislocated to the left, and downward. Sometimes there are visible pulsations close to the sternal border on either side; at other times the whole chest throbs.

After dilatation of the right ventricle occurs there is generally a pulsation in the epigastrium, while at the same time pulsations are visible in the cervical veins. In old people and in arteriosclerotic cases these extensive pulsations are not commonly met with. In cases due to relative insufficiency the evidence of dilatation as shown by the projection of the apex-beat is not prominent. It may be scarcely noticeable outside of the nipple line. When there is evidence of broken compensation, there is also marked dilatation of the jugular bulb above the right sterno-clavicular junction.

Palpation.—The impulse is heaving. A systolic thrill is sometimes felt, particularly in children, but is relatively infrequent. If auricular fibrillation is present the beat is, of course, irregular. The pulse and apex-beat are much in accord both as to strength and regularity; the pulse is usually small, easily compressible, and regular unless auricular fibrillation is present, in which case it becomes rapid and irregular. The number of beats which are counted at the wrist is much smaller than the number of beats counted with the stethoscope. This is known as *pulse deficit.*

Percussion.—Dulness is increased to the left, often over as far as the anterior axillary line, and to the right as much as one inch to the right of the sternum. But such an enlargement is unusual. The cardiac dulness is increased more laterally than in the vertical direction. In most cases that are well advanced, the upper border of cardiac dulness commences about as high as the third intercostal space. This upward extension of dulness is due to enlargement of the conus arteriosus of the right ventricle.

Auscultation.—The diagnosis of mitral regurgitation is commonly made on the basis of auscultation. At the point of the apical impulse there is a systolic murmur which may either follow or entirely replace the first sound. Its character varies, but it is frequently a blowing murmur. The murmur can usually be traced outward toward the axilla. It is transmitted to this region because the vibration is transmitted through the papillary muscles of the left ventricle down to the apex, thus making a solid conducting medium down almost to the chest-wall, and as the tip of the left ventricle is nearer to the surface in the axilla than on the front of the chest-wall. Theoretically it should be easily possible to hear the murmur better here than in front. Sometimes it is well heard at the middle of the posterior border of the scapula, the sound being then transmitted by the vertebræ from the base of the ventricle. In other cases it may be better heard to the right of the nipple line than at the apex. These variations in the intensity of the murmur are due to the varying contents and relations of the structures in the individual chests. In some cases the lung covers portions of the heart which are usually exposed, or again the bony framework presents some anomalies which interfere with conduction.

The pulmonary second sound is accentuated or frequently reduplicated. It is best heard over the second interspace at the left edge of the sternum.

When there is a failure of compensation one often hears another murmur at the same time over the lower part of the sternum. This is due to tricuspid regurgitation. It is softer than the mitral murmur.

Special Examination. — *Blood-pressure.* — In uncomplicated cases there is nothing characteristic in the blood-pressure. Very frequently it is lower than normal.

Pulse-tracing.—There is nothing characteristic in the pulse-tracing of uncomplicated mitral regurgitation.

Electrocardiogram.—In uncomplicated early cases there is no information to be obtained. When evidences of failing compensation are present, signs of right side hypertrophy are also found because the R-wave in lead 1 is directed downward instead of upward as is the case in normal individuals.

X-ray Findings.—In early compensated cases the *x*-ray shows a uniform smooth circular enlargement to the left. Later it is often oval in shape. In advanced disease the picture is fairly typical. The arch of the aorta is frequently pronounced, but the rest of the heart is globular. It is an ovoid in which the longest axis lies diagonally.

Diagnosis.—One frequently meets with a patient who presents a group of general symptoms indicative of no local or specific disease, such as increased temperature, headache, dyspnea, cough, muscular pain, etc. On making a physical examination, a mitral regurgitant murmur is discovered, and because of character, transmission, and history of previous rheumatic fever, it may be considered to be a true organic lesion. The question arises as to whether the symptoms are due here to fresh attack of endocarditis, with broken compensation, or to another disease, the mitral regurgitation being coincident. This is often a difficult problem. If on auscultation one finds behind the left scapula a large number of fine crackles after the patient has been lying on his back, or, if, on slight exertion, there is manifest dyspnea which was not previously present, and if we can exclude pneumonia and pleurisy, we are justified in considering that the symptoms are due to the valvular disease rather than to some other general disease. Usually, if the heart is at fault, close questioning will show that there have been other minor symptoms in the immediate past. In general, mitral regurgitation is likely to be mistaken for (1) pulmonary tuberculosis, (2) neurasthenia due to any cause, (3) cirrhosis of the liver, (4) chronic nephritis. The latter two have been discussed previously under Symptomatology. When the murmur is so faint that it cannot well be heard the disease is not infrequently mistaken for *pulmonary tuberculosis.* The early symptoms of both diseases are similar: dyspnea on exertion, digestive complaints, slight cough, clubbing of the fingers, neurasthenic symptoms, loss of weight, and in the presence of a fresh attack of endocarditis or bronchitis, a temperature of 101° F. (38.33° C.) or over. Whenever valvular disease is the cause, careful auscultation with the patient lying on his back (and this should be the method of choice in examining any cardiac patient) will sooner or later reveal a systolic murmur. It may not be present on the first examination, but it will be evident in a day or two. Here, at times, only the examination of the sputa will settle the question. A history of previous rheumatic fever speaks for valvular disease. Rheumatic fever is very uncommon in patients suffering from tuberculosis. It may be argued that a mitral regurgitant murmur may coëxist with pulmonary tuberculosis. It is true that this is possible but it is the exception and not the rule, and in the presence of a mitral cardiac murmur without any distinctive and positive evidences of tuberculosis, one is justified in considering the endocarditis as the most likely cause of the symptoms. The presence of hemorrhage adds a confusing element, but the hemorrhage of cardiac disease is usually a single cycle one, that is, the blood is brought up following some exertion and does not recur, whereas in tuberculosis blood-stained sputa are usually present for several days following the initial hemoptysis. A slight rise in temperature within a few days after the hemorrhage is the rule in tuberculosis. Also, the minor symptoms, such as loss of appetite and digestive complaints, are also commonly aggravated after the hemorrhage, whereas in heart disease the patient generally feels better after the hemorrhage.

Finally, in every case in which there is the slightest doubt the sputa should be examined. Fluoroscopy is sometimes of confirmatory value. The heart of mitral disease shows some enlargement, whereas the typical heart of tuberculosis is characterized by extreme smallness and by its lying in the vertical position; in fact, some roentgenographers assume the diagnosis of tuberculosis on the presence of a few signs and on the small heart alone.

The neurasthenic syndrome so often present in cardiac disease suggests an ordinary nerve exhaustion or *neurasthenia,* and this is a frequent error. The knowledge that there is always a cause for neurasthenia and that chronic endocarditis is a frequent cause of this group of symptoms should be sufficient to prevent the error.

When a systolic *murmur* is heard over the mitral area the question at once arises as to whether it is due to disease of the valves, or to some temporary cause (functional) or whether it is accidental, due to adhesions, etc.

Inspection and palpation are good guides in estimating whether or not the systolic murmur is an organic murmur. If the apex-beat is outside of its normal location and very powerful, then certainly an organic lesion is present. On the other hand, an organic lesion may be present without a marked dislocation of the apex-beat. In addition to organic valvular disease the murmur may be due to dilatation of the left ventricle without organic changes in the valve, being secondary to (1) aortic disease, (2) increased blood-pressure in chronic nephritis, arteriosclerosis, myocarditis and pericarditis, (3) over-exertion, acute fevers, acute nephritis, cachexia.

Indications of organic disease are the following:

(1) The loudness or roughness of the murmur. It is very seldom that a rough, loud, systolic murmur in this location is due to anything else than an organic change in the valve. The following exception to this rule should be noted: the systolic murmur, so commonly heard at the base and apex of the patients suffering from a general arterio-

sclerosis, is usually due to an arteriosclerotic process in the aorta or at the aortic orifice and is transmitted to the apex of decompensation. It is true that such a murmur is often associated with symptoms, but autopsy commonly fails to reveal organic mitral changes.

(2) Enlargement of the heart as evidenced by a displaced apex-beat and increase in the area of cardiac dulness.

(3) A history of rheumatic fever or of chorea.

(4) Age of the patient. In children, except when found in acute fever, it is most likely to be due to previous rheumatic fever. The absence of fever will rule out the murmur due to the other infection.

Indications of mitral regurgitation due to functional dilatation of the left ventricle are the following:

(1) Age of the patient. Myocarditis is not commonly developed before middle life.

(2) Presence of other evidences of arteriosclerosis or of chronic nephritis.

(3) Presence of a non-rheumatic aortic obstruction or regurgitation with hypertrophy and dilatation of the left ventricle.

(4) Dyspnea on exertion without any apparent cardiac lesion. This is likely to be due to myocarditis. Furthermore, the dilatation of the left ventricle may, in rare cases, be due to adherent pericardium, and the systolic murmur heard may also be due to anemia, or to cachexia. In the latter instances it is localized in the mitral area and is not conducted to the axilla or back, and there is no cardiac enlargement.

Furthermore, there is in addition a systolic murmur over the pulmonary area and also a venous hum in the neck. Such murmurs are quite frequent in the fevers of small children.

In general, in children a murmur should not be considered of organic significance when it occurs in non-rheumatic fevers, unless it is very loud and very distinct.

The murmur of mitral regurgitation is seldom mistaken for that of any other organic cardiac murmur, because it is distinctive and usually localized at the apex. It is true that some observers claim to have occasionally heard it better at the base of the heart, but the mass of critical observation is against these findings. When the murmur is due to a relative insufficiency, it disappears under rest and digitalis as soon as the temporary overstrain or dilatation is recovered from, whereas, if the murmur is due to changes in the valves themselves due to organic disease, the murmur will increase in intensity when the muscle regains its strength.

The cardiorespiratory murmurs give most trouble in differentiation, and yet they are comparatively easy to rule out if one continually thinks of the possibility of such a murmur. They are frequently found at the apex, and their chief characteristic is that they vary with the respiratory cycle. They are usually louder during inspiration, and they are usually lost at the apex when the patient holds his breath; on the other hand, they may only be present under just such circumstances. They undergo alterations with the changes in the position of the patient. Of course, this is also true of organic murmurs, but the cardiorespiratory murmurs give one the impression of being nearer to the ear than endocardial murmurs do. The murmur commences suddenly and ends suddenly. It is not conducted in the direction of the axilla, but extends along the lower portion of the chest between the apex and the sternum. A congenital systolic bruit is sometimes a stumbling-block in the diagnosis of cardiac disease, particularly in children. It usually occurs in connection with a normal apex-beat and dulness which extends up as far as the second rib and to the right of the sternum. Because of the thinness of the chest-wall in these children this dulness is very striking when it is looked for, and is of much value in the diagnosis of the congenital lesion. In rare cases a patent ductus arteriosus or an acute pericarditis may produce a murmur that is puzzling, but its nearness to the ear, and the to and fro character of the murmur, are sufficient to rule out endocardial disease. It must be remembered that in the cases of pericarditis an endocarditis is also frequently present. A loud systolic murmur of tricuspid insufficiency due to primary mitral stenosis may be confusing, but here the murmur is never as clear over the mitral region as over the tricuspid area; furthermore, the presence of liver pulsation and a throbbing jugular vein, with other evidences of tricuspid insufficiency, will usually decide. Of course, the combination of mitral stenosis and mitral regurgitation is almost the rule in such cases.

Prognosis.—The favorable cases are such as have existed for some years without any of the symptoms of heart-failure.

The eventual outlook is better in mitral regurgitation than in any other lesion. Such a large proportion of these cases are due to relative insufficiency that practically complete recovery frequently takes place.

In the average organic cases at least half a dozen breaks in compensation usually occur before the serious stage of the disease appears. Frequently the intervals between such breaks in compensation may last for months and even years, so that patients frequently live for ten or twenty years after having had what seemed to be a fatal illness with general anasarca, dyspnea, etc.

In no condition in life is the patient so frequently brought to the brink of death without actually succumbing as in mitral regurgitation.

Dyspnea on exercise is the best index of the extent of the lesion. If strenuous exercise can be indulged in without any evidence of dyspnea, there is no reason for regarding the lesion with any immediate concern. The outlook in any case is in exact proportion to the reaction from exercise. Patients regularly recover from early attacks of dyspnea. However, when dyspnea occurs in a patient who has already been in bed for several days the outlook is extremely grave.

As compared with the muscular damage done by the agent causing the valve lesion—whether it is rheumatic fever, arteriosclerosis or lues

—the valve lesion itself is of relatively slight importance from a prognostic standpoint, and there is a strong probability that a mitral murmur present in acute rheumatic fever, and not very marked, will, in one-third of the cases, disappear within six months. On the other hand, a murmur which has lasted for a year will not disappear. The murmur following chorea disappears in about one-half of the cases.

In the case of mitral regurgitation due to rheumatic fever the outlook is better than that due to any other disease.

When syphilis is a cause—and this is not frequent in mitral regurgitation—some permanent improvement may occur under treatment, provided the lesion is recognized sufficiently early, before extensive damage has been done. But on the whole satisfactory medication is disappointing if one expects the same results that are to be obtained in syphilitic lesions of the skin and of other parts of the body.

Whenever there is a high blood-pressure with regurgitation and loss of compensation, the dilatation becomes a serious matter. The already damaged heart-muscle, in addition to its ordinary work, must overcome the peripheral resistance thus added. This soon results in a further break in compensation, so that in mitral regurgitation plus high blood-pressure, once there is a loss in compensation the outlook is gloomy.

If this high blood-pressure can be controlled by change in habits, food, etc., of course the outlook is correspondingly brighter, so that when this combination is found, one should be careful in giving an unfavorable prognosis at the first examination.

A very great fall in blood-pressure is of serious import. This is true even if the blood-pressure has been quite high, say 180 or over, at some time. The association of organic mitral regurgitation with a kidney lesion, especially if marked dyspnea is present, is an extremely grave combination.

The accentuation of the second pulmonic sound is the surest way of estimating the degree of back-pressure in the pulmonary circuit and is therefore an index of the condition of the left side of the heart. This powerful accentuation may go on for years provided no intercurrent infection takes place, and the patient may not be any worse than when first seen.

This accentuation is usually accompanied by some dyspnea on exercise. A good, full pulse without atheroma is a favorable sign, because it usually indicates a good heart-muscle.

Murmur.—No matter what the character of the murmur may be, with the apex in a normal position or nearly so, there is no immediate danger. Likewise, a persistence of the first sound indicates that there is no likelihood of immediate termination. In advanced cases the murmur takes the place of the first sound, and this makes the outlook worse. In general a loud murmur offers a better outlook than a faint, weak murmur. The murmur with the worst prognosis is a short whiff, changing in strength and duration with each beat.

There is no physical sign so terrifying to the young practitioner as the irregularity of the pulse of auricular fibrillation. It is positive proof of a bad muscle, yet many such patients do live with this irregular pulse for a decade, with little or no distress, and as far as one can ascertain either from a study of the sounds or of the tracings, there is no way of stating when any serious consequences will follow. Of course, this does not mean that it is not a serious lesion. It is always associated with muscular and usually with valvular changes which render the heart far from normal. But if the lesion has existed for some months without any apparent ill effect as such, then one cannot consider that the altered rhythm offers us any basis for an immediate prognosis, although we do know that eventually decompensation is almost certain to follow.

Treatment is also more satisfactory in this particular lesion than in any other.

The common irregularity associated with extra systole must not be mistaken for auricular fibrillation. Ordinarily in sound hearts this extra systole has no evil prognostic meaning. When it occurs for the first time in the course of mitral diseases it may not be dismissed so readily. Auricular extrasystoles are often the forerunner of auricular fibrillation, and without instrumental means it is impossible to distinguish them from the relatively harmless ventricular variety. The extrasystole due to digitalis toxemia must always be kept in mind.

There are some differences between the prognosis of mitral regurgitation in children and that in adults. It is fair to assume that a lesion causing much deformity of the valve in a child has a serious prognosis. As a normal heart enlarges, the cavities of the heart must correspondingly enlarge and the valve must enlarge and lengthen from the base to the free edge. The deformed and sclerosed valve can scarcely be expected to do this, and the separation between the valve edges must grow correspondingly greater, forming an increased regurgitation as the heart grows older. After the first signs of broken compensation in children, the downward progress is more rapid as a rule, inasmuch as the adult has noticed minor symptoms much earlier than the child and has taken better care of himself.

Among these early signs in children that are frequently overlooked is a *loss of mental power* and of emotional control. The child is irritable and does not get on well at school; but the first symptoms to attract attention are usually the major symptoms, dyspnea, dropsy and hemorrhage.

With the failure of compensation there is rapid loss of weight, and appetite, and other distinctive symptoms.

The ease with which intercurrent infections set up acute endocarditis renders the prognosis always less favorable in children. This is the lesion most commonly met with in children, and the younger the child the worse the outlook.

If there has been a marked break in compensation before puberty, adult life is rarely attained, many of the patients dying in consequence of an acute endocarditis. On the other hand children who have not had fresh attacks of rheumatic fever and frequent head colds very generally go on through life with little or no distress except palpitation and dyspnea on severe exertion. So in the absence of evidences of broken compensation one is justified in giving a fairly favorable prognosis as to the outlook in cases of mitral regurgitations in early childhood.

Mitral regurgitation *as such* seldom kills. Usually stenosis is added before the fatal issue is imminent. This combination becomes evident from:

(1) The increased loudness of the systolic murmurs, with strong apex beat.
(2) Accentuation of the second pulmonic sound at the apex.
(3) Reduplication of the second sound.
(4) A murmur with the second part of the reduplication.

When this group is persistent, mitral stenosis has been added and the outlook is growing darker.

Mode of Death.—The sufferer from mitral disease nearly always dies eventually from the complications, particularly those in the lungs, such as bronchitis or pneumonia, sometimes from diarrhea due to croupous enteritis. These patients usually die in bed. Cold weather is particularly fatal to them, even though they are not exposed to it. Sudden death in cardiac patients who are exposed to the cold during a cold wave is by no means uncommon. A prolonged hot spell is apt to be the final cause of death in a cardiac patient who is ill in bed during the summer. This is particularly true if there is much humidity. A fair proportion of these patients die at stool, possibly because of the exertion. The presence of marked mental symptoms, particularly delirium and hallucinations, in mitral diseases, are among the most certain signs of approaching death. An up and down movement of the abdomen exactly opposite in time to that of the chest in inspiration and expiration in a manifestly ill cardiac patient generally indicates approaching death. The patient seldom recovers from stupor and coma in mitral disease, but death in coma is not relatively common in these patients. Persistent vomiting, diarrhea or dysentery are usually grave symptoms in a cardiac patient with broken compensation. Rapid breathing, following a Cheyne-Stokes respiration, is generally an indication of a fatal termination. Long apneic intervals in the Cheyne-Stokes phenomenon are also of bad omen. The fact that a patient who has suffered from a long period of dyspnea is suddenly able to lie down flat and sleep, in the absence of any other improvement, is generally a sign of approaching death. A low-lying heart flat on the diaphragm, as shown by x-ray, is found in the type of patient who is apt to die suddenly. Sudden death without any warning is an extremely rare event in mitral regurgitation, except when arteriosclerosis is the cause of the lesion.

Pathology.—PATHOLOGICAL PHYSIOLOGY.—The changes found postmortem are sclerotic, ulcerative, or vegetative alterations of the cusps or often of the chordæ tendineæ. Often there is infiltration or shortening of these structures. The most common evidence of relative insufficiency is a uniform thickening of the free valvular margin with some contraction.

In the early stages the left auricle is hypertrophied; in the latter stage it is dilated and atrophied. The auricular surface of the anterior cusp usually shows the most marked changes.

The early microscopical evidence of rheumatic endocarditis consists of small nodules on the edges of the cusp. When changes occur later they are for the most part due to involvement of the chordæ tendineæ, which are thickened or shortened. Thus rheumatic disease of the mitral valve is in its serious aspects a disease of the chordæ tendineæ. The mitral valves fail to prevent leakage, either because of organic changes or because of failure of tonicity of the auricular muscular sphincter (functional). This lack of tonicity on the part of the sphincter may be due to degeneration of the muscle or to pure weakness.

Any great enlargement of the ventricle with the consequent shortening of the papillary muscles must permit of some regurgitation. The leaks occurring at the mitral valve as a result of muscular weakness are due, in one group of mild cases, to weakness of the papillary muscles, which allow the valve to be slightly elevated, thus permitting a small stream of blood to pass by it; or, because of the great dilatation of the left ventricle, the mitral orifice becomes larger and wider than the area of valve surface, so that considerable leakage occurs.

This functional insufficiency occurs in toxemia, overstrain, anemia, and, in the case of convalescents, from acute disease. It is the added functional lesion, or, to be more exact, the result of muscular insufficiency, which is finally responsible for the breakdown in most valve lesions. It is the exception for valve changes in themselves to be responsible for the loss of compensation.

When the condition is due to vegetations, they prevent coöperation of the valves and permit the blood to regurgitate.

The part that functional insufficiency plays in cardiac pathology is evident in the rapid recovery under rest in most cases of cardiac failure, even though the organic lesions remain the same. This functional regurgitation explains why a case presenting all of the evidences of mitral regurgitation during life may yet show no organic change postmortem. In a majority of the cases of organic regurgitation there is an added obstruction or stenosis.

MITRAL STENOSIS

Etiology.—There is a growing feeling among cardiologists the world over that mitral stenosis is the serious mitral lesion, and that mitral regurgitation, when it becomes immediately serious, is so because of an added mitral stenosis. Therefore, much of the description of the symptomatology of mitral stenosis is applicable to mitral regurgitation as well. The lesion is much more common in women than in men.

Probably 75 per cent. of all the cases met with in early life are due to a previous *rheumatic fever*. *Chorea* is the next most frequent cause. After this, *tonsillitis*, and, later in life, *arteriosclerosis* and *syphilis*, follow in order of frequency. There is no doubt that even in primary cases associated with rheumatic fever there are two types of cases. In the endocarditis which usually accompanies well-defined rheumatic fever, the area involved by the inflammation is considerable. The whole inside of the auricle and ventricle, and usually the muscle as well, are to some extent infiltrated with small areas of round-cell inflammation. As a result of this contraction following this, of course, there is shortening of the chordæ tendineæ and retraction of the mitral leaflets, so that there is constriction and regurgitation. This is the common type. When inflammation is more limited and involves the mitral ring on its auricular aspect, the process is slower and the whole course of the disease less striking. In this type we are apt to find occasional pains in the joints or muscles, but no well-defined attack of rheumatic fever. It is in these cases that one most frequently finds the classical picture of mitral stenosis. Many of the patients think so lightly of their pains and aches that they deny ever having had rheumatic fever.

The type of mitral stenosis met with in Russian emigrants, particularly among women, deserves particular attention, as it is becoming a frequent clinical entity in this country. In many respects the history resembles that of the second class of cases mentioned above. There is this exception, however, that the disease, once the symptoms become noted, appears to progress more rapidly than is usually the case with those following rheumatic fever.

Symptomatology.—CLINICAL HISTORY.—The subject suffering from mitral stenosis presents one of two more or less distinct clinical pictures. Either the condition is a primary affection, or it is associated with or secondary to mitral regurgitation. In the latter instance the picture is usually dominated by that of the accompanying regurgitant lesion.

In the primary cases, certain types of patients predominate. Why this is so it is difficult to explain. The patient is seldom very tall or large. The women are, however, often quite stout and florid. There is a yellowish pallor of the forehead and around the nose and mouth. This is frequently accentuated by the presence of red cheeks. As the disease advances, this congestion acquires a purplish hue which enables one at times to make a guess at a glance as to the lesion present. In children, the subjects of mitral stenosis following attacks of rheumatic fever, there is often a failure of development. They are sickly, pale and anemic, and cannot compete with other children because of the shortness of breath that is present. They are subject to frequent attacks of bronchitis, and seldom live to be more than thirty years of age. In these primary cases the patient goes on for years with few symptoms, and even these are taken as a matter of course. Shortness of breath, or palpitation on unusual exertion, or sticking pains over the heart and a choking sensation in the throat, are accounted as the portion or lot of the female sex, among whom the disease is most common. These symptoms are much more marked at the menstrual period, but are rarely of sufficient severity to require medical aid. Furthermore, these patients are naturally optimistic and seldom complain of their distress, which they have come to count as a part and portion of their existence. As years go on dyspnea is induced by less and less effort. A short single effort cough is generally present, and is particularly noticeable when the patient is climbing stairs or during any physical or mental exertion, such as beginning a conversation, etc. Nose-bleed and hemoptysis on mental or physical exertion are not uncommon. Such patients are particularly susceptible to attacks of bronchitis during the winter months; acute infections, as well as fresh attacks of endocarditis, associated with head colds, pharyngitis, etc., are very common. These attacks are usually associated with increased temperature (from 100° F. to 102° F., or 37.77° to 38.88° C.), and persist for from one to two weeks. They are nearly always accompanied by an aggravation of the symptoms previously complained of, and bring about a temporary loss of compensation, sometimes so severe as to threaten life. Recovery usually ensues, and for a period of months, and even years, the patient is apparently as well as ever, except that the dyspnea is more easily induced than it was formerly. Pains in the chest resembling angina pectoris are occasionally complained of following severe exertion. Recovery from such attacks, in those whose disease is of rheumatic origin, may be generally prophesied. When there is a complete failure in compensation, the symptoms are largely those described under Mitral Regurgitation. The condition is first evidenced by signs of stasis in the lungs. The attacks of shortness of breath become more frequent, and later on are more or less continuous. At first these dyspneic attacks, which occur independently or on exertion, are present only during the night from twelve to four o'clock; later they appear during the day as well. Sleep is impossible, except for short naps. Cheyne-Stokes breathing is a frequent accompaniment, especially in those past middle life. Sooner or later most of the other symptoms of broken compensation associated with mitral regurgitation and tricuspid regurgitation appear. General dropsy and venous engorgement, although early symptoms in mitral regurgitation, are comparatively late symptoms in mitral stenosis. Marked enlargement of the liver, and ascites, are the rule in advanced cases. Ascites occurs more early in the broken compensation of mitral stenosis than in that of mitral regurgitation. Cough is present at intervals throughout the course of the disease. The sputum is frequently reddish in color. It must be distinguished from the bloody expectoration of the attacks of hemoptysis, which are described elsewhere. This red color is due to hemosiderin, a yellowish-brown pigment contained in large nucleated cells, the so-called heart-failure cells.

These are the results of brown induration of the lungs consequent on the long-continued back-pressure in the lung. These cells occur in other forms of endocarditis, but they are more common in old mitral stenotic lesions than in any other pathologic condition. The occasional accompaniment of paralysis of the recurrent laryngeal nerve, as described under Pathology, should be kept in mind as a possible cause of the hoarseness and loss of voice. Auricular fibrillation is more common in mitral stenosis than with any other lesion, and develops sooner or later in the majority of cases during the course of this disease. Attacks of paroxysmal tachycardia sometimes take the place of auricular fibrillation.

PHYSICAL FINDINGS.—*Inspection.*—The facies is sometimes suggestive. Pulsation is usually prominent over the region of the apex-beat. It may also be evident near the sternum in the second and third left interspace. When compensation is broken it is visible in the epigastrium.

Such pulsations are much more common in childhood because the chest-wall is more pliable. A convenient way of demonstrating this is by sticking small pieces of paper or cardboard that have been folded at right angles to resemble the letter L perpendicularly over the apex and base of the heart. In this manner it can be easily shown that both of these regions do not raise the paper at the same time. The lower one moves with the ventricle while the movement of the other corresponds to that of the auricle. Sometimes retraction of the third, fourth and fifth interspaces may be seen corresponding to each systole. Bulging of the chest-wall close to the sternum and in the epigastrium is occasionally quite marked in children. Should pulsation be present over this area and absent at the nipple, the fact indicates hypertrophy of the right ventricle. In these cases this is the chief impulse, and it is more marked than over the left ventricle. If adherent pericarditis can be ruled out, Hare thinks that there is strong evidence in support of the causal rôle of mitral stenosis in the production of this pathology.

Palpation.—On palpation a pulsation is felt corresponding to the apex-beat; this is usually strong, sudden, short or tapping. Also, in thin chests, a pulsation may be felt near the sternum in the second and third left interspaces. The *thrill* is one of the most valuable points in diagnosis. It is presystolic in time and is best felt in the fourth or fifth interspace near the line of the nipple. The thrill stops suddenly on systole. If aortic regurgitation can be excluded, the diagnosis of mitral stenosis may be made on this basis alone. The thrill varies in the same patient, being present at one time and absent a few hours later. Exercise and change of posture will often serve to elicit it. When the thrill is not felt in either the erect or the horizontal position, the patient should be turned over on his stomach and the apex palpated. The thrill is usually most marked during expiration. It frequently disappears when there are marked evidences of dilatation. The heaving impulse near the line of costal cartilages on the left side, not palpable at the nipple, is a counterpart of the signs mentioned above under Inspection. The cardiac impulse itself frequently gives one the sensation as if a jet of liquid were projected against the hand. Pulsation of the edge of the liver is due to back-pressure from the tricuspid regurgitation, a common consequent of mitral stenosis. One must not mistake the impulse transmitted from a dilated heart.

Percussion.—Early in the disease there is very little evidence of enlargement beyond the right border of the sternum; when this occurs it is the first evidence obtainable on percussion. When dulness is present on the left side it is quite high up. Later on in the course of the disease the dulness is, of course, increased to the left and beyond the nipple, and may extend as high as the third rib. This dulness is largely due to cardiac dilatation, secondary to the stenosis. It corresponds to a short wide oval and may be verified by x-ray examination.

Auscultation.—The murmur is the most characteristic physical sign. This begins during the diastole. It gradually increases while the auricle contracts, and becomes most noticeable just before systole; hence it is called presystolic. The sound of the murmur is *crescendo* in character, and for purposes of instruction may be so described, but the electrocardiogram shows that this *crescendo* quality is due to its proximity to the loud, slapping first sound. Generally the murmur can only be heard in a restricted area. It is usually on a line drawn along the fifth rib from the sternum to the nipple. Sometimes this area is not more than an inch in diameter. On other occasions it may be heard all over the heart, but in general its audibility is the least extensive of all murmurs. It is commonly a harsh vibrating murmur or a thunder-like rumble. The time of the murmur changes from presystolic to mid-diastolic, or even to early diastolic, depending upon conditions within the heart. When compensation is well established it is presystolic; when compensation is broken it is often diastolic. As cicatrization goes on the murmur changes. Even before the murmur is appreciated by the ear a presystolic thrill may be felt. As has been stated with regard to the thrill the murmur changes frequently. If the damage to the valve is recent the murmur is more likely to change. The older it is the more constant. When compensation occurs it often becomes diastolic again, and as the disease progresses one hears the murmur beginning just at the end of the second sound, and often filling the entire interval. It is important to recognize the fact that this murmur is frequently diastolic instead of presystolic, inasmuch as it is so commonly mistaken for the murmur of aortic regurgitation. This is particularly true when the sounds are quite loud and transmitted for a considerable distance away from the usual area. When in doubt as to the timing of the murmur, the examiner should palpate the apex-beat for the systolic shock. It will thus be easy to follow the murmur up to the shock. Sometimes presystolic and diastolic murmurs are heard in the same case, but usually the presystolic murmur disappears on the appearance of the diastolic. Often both disappear on the occurrence of dilatation, and a systolic murmur alone is audible. The diastolic murmurs of mitral stenosis do not have the rasping character of the presystolic, but are soft or blowing in type. There is a growing feeling that the murmur is always present during diastole, and its audibility, during presystole in one case, and in diastole in another, depends upon modifying circumstances. The diastolic murmurs are best heard near the sternum along the fourth rib, whereas the *crescendo* has its home near the nipple. This is particularly so in children. It is also very noticeable in gallop rhythm that the murmur is always tagged on to the third sound near the sternum. To recapitulate, we may put in order of frequency, a presystolic, a mid-diastolic, or a mid-diastolic and presystolic, or a diastolic murmur occupying the whole of the ventricular diastole. Sometimes the murmur can only be elicited by having the patient lie on his abdomen and auscultating while he is in this posture. The murmur of mitral stenosis is often accompanied by a mitral systolic murmur, inasmuch as regurgitation frequently occurs through the narrow rigid orifice. The inhalation of amyl nitrite occasionally makes the stenotic murmur audible. A Bell stethoscope is sometimes better than the usual Bowles type, now in common use. The murmur is often best heard with the patient in the prone position.

The second sign of value on auscultation is the accentuation of the pulmonary second sound. This is best heard at the third interspace on the left side. It is caused by the high blood-pressure in the pulmonary artery, which is produced by the back-pressure of the blood in the lungs. Instead of this accentuation, one frequently hears a reduplication of the second sound. It is best heard at the base, although in a strongly acting heart it may also be audible at the apex. It is due to the failure of the aortic and pulmonary valves to close synchronously. It is produced as follows: When the pressure in a pulmonary circulation is proportionately much above normal the pulmonary semilunar valve closes before the aortic; then the first sound of the reduplication is due to the closure of the pulmonary valve, while the second portion of the reduplication is due to closure of the aortic valve. This is not pathognomonic of mitral stenosis, as it occurs in other conditions. It is present in about 65 per cent. of the cases of mitral stenosis. At the end of the second part of the reduplication, one often hears a murmur. This murmur often lasts throughout the whole of the diastole and cannot be distinguished from the presystolic murmur if it is still present. These sounds may be imitated by the phrase "la-rup-de-de." The "la" corresponds to the presystolic murmur, "rup" to the sharp snapping first sound, "de-de" to the reduplication, in which reduplication the second sound "de" is somewhat longer and often terminates in a murmur. This third sound is sometimes spoken of as the third sound of the heart. The signs thus far enumerated are present either alone or together in a classical case, and the diagnosis may be made on the basis of almost any one of them, certainly when any two are present. However, the diagnosis, especially in early cases, is not always so easily made. There are several other signs which are of considerable value in directing one's attention to the presence of a possible mitral stenosis. The chief among these is a slapping first sound heard at the apex. This is often the only phenomenon to call attention to the possibility of mitral stenosis. This first sound is so entirely different from that of any other condition that it attracts attention at once. It is only in neurasthenia that one meets with such a forcible beat, and then other points, such as the lack of accentuation of the second sound, are sufficient to rule out such a condition. This phenomenon is not present in all cases of mitral stenosis, but it is present in a large percentage of cases and it remains even after the onset of broken compensation. It is lacking usually if much regurgitation is present. It is only heard over a small area about the apex. Another evidence that mitral stenosis is probable is the presence of auricular fibrillation, for this is the disease *par excellence* wherein one finds this irregularity. Usually when auricular fibrillation develops the presystolic murmur disappears. The reason for this is that in fibrillation the auricle is nothing more than the continuation of the vena cava. There is no effort to contract in this part of the heart, so that no propelling force is exercised in forcing the blood through the narrow orifice and thus producing murmur. There is another diastolic murmur which is frequently heard as a secondary murmur in mitral stenosis. It is best heard in the left third and fourth interspaces along the left border of the sternum. By some clinicians it is interpreted as being due to a relative insufficiency of the pulmonary valves due to the high pressure in the pulmonary artery and dilatation of the right ventricle. It was described by Graham Steele, and is known as the Graham Steele murmur.

Pulse.—In the past there has been a wide divergence in the description of the pulse of mitral stenosis, one group of observers stating that it is a small full pulse occurring between beats, and that it is characterized by moderately high tension, so that it can be rolled under the finger between the beats. Others contend that it is small, soft, and characterized by lower tension (mitral pulse). As a matter of fact either of these conditions may be present in mitral stenosis.

Recent observations show that rheumatic fever affects the kidneys as well as the heart, in a large percentage of cases, and this would explain the pulse as described in the first group, whereas in the second group there is no organic involvement of the kidney.

The development of auricular fibrillation can often be traced from the beginning of irregularity. There is commonly an inequality in the force of the beats without any decided change in the rhythm. Thus some of the beats fail to reach the wrist, but the rhythm is still constant, so that the heart-beats may be regular and yet the pulse at the wrist irregular. Later the irregularity in rhythm becomes marked over the heart as well, as auricular fibrillation becomes established.

Special Findings.—*Blood-pressure.*—There is no characteristic change in blood-pressure. The pulse-pressure is frequently diminished.

Pulse-tracing.—There is no pulse-tracing which is characteristic of the disease. However, when fibrillation appears, as it does so frequently in mitral stenosis, the tracing is quite characteristic.

Electrocardiogram.—In some cases of mitral stenosis the enlargement of the P-wave is an indication of auricular hypertrophy. Such waves are often one-fifth instead of one-tenth as high as the R-wave. They are often prolonged and have a bifurcated or flattened summit.

The hypertrophy of the right ventricle which accompanies such cases is indicated by the direction of the leads of the electrocardiogram. Normally the R-wave is directed upward in 3 leads, whereas in mitral stenosis R 1 is directed downward, while the R-wave of lead 2 is smaller than that of lead 3. This fact is of some value in differentiating those cases of mitral stenosis in which diastolic and presystolic murmurs are present, due to aortic regurgitation with an Austin Flint murmur.

X-ray Findings.—Early in the case orthodiagrams show a relatively small oval with a vertical axis; the enlargement of the left auricle may be evident in the picture, and later on in the disease the addition of mitral regurgitation produces a picture indistinguishable from that of the latter disease alone.

Diagnosis. — PHYSICAL SIGNS. — In simple, uncomplicated primary mitral stenosis there is as a rule little difficulty in making a diagnosis. The characteristic *crescendo* murmur, once well fixed in the mind, is seldom forgotten. With the thrill and marked accentuation or reduplication of the pulmonic second sound there is sufficient evidence upon which to base a diagnosis, and where there is any doubt, the presence of the slapping first sound easily clinches it. But all cases of mitral stenosis do not present the presystolic murmur nor the other characteristics; on the contrary, the murmur is often diastolic in time and may be heard over a more extended area than that over which the murmur of mitral stenosis is usually distributed. The other distinguishing findings may be in abeyance on the day of examination. For that reason, of all the common heart lesions mitral stenosis is the one which is most likely to escape detection. The murmur itself is the most uncertain and variable of all the cardiac murmurs. In doubtful cases it is sometimes present and absent on the same day, even changing with the position of the patient. Furthermore, it is frequently accompanied by the murmur of regurgitation, and the latter may be so loud that it obscures the murmur of stenosis.

In general there are five other conditions producing a diastolic murmur over the heart, and while the tone of each is usually different, the extent of transmission is sometimes such that the practitioner is in doubt as to which category the murmur belongs. These murmurs are:

(1) That of aortic regurgitation, usually best heard at the second right intercostal space or at the midsternum opposite the third costal cartilage and well transmitted down along the right or left border of the sternum.

(2) The Graham Steele murmur, best heard over the left third and fourth interspaces near the sternum and not transmitted.

(3) The murmur of pulmonary regurgitation, audible in the same location as the Graham Steele murmur, and in the present state of our knowledge, indistinguishable from it.

(4) Tricuspid stenosis, an extremely rare murmur, best heard on the right side of the sternum out toward the right nipple.

(5) The so-called Austin Flint murmur or diastolic murmur heard at the apex in some cases of advanced aortic regurgitation.

The question which causes most difficulty is the differentiation between the murmur of aortic regurgitation and that of mitral stenosis. This is one of the most difficult diagnostic problems, particularly when the other signs of aortic disease are not in evidence.

The murmur of aortic regurgitation is confined almost entirely to the base of the heart, and is transmitted upward and downward, yet occasionally it is quite distinct over the mitral area and beyond. But its point of maximum intensity is always up near the second costal cartilage, whereas the point of maximum intensity of mitral stenosis is always down in the neighborhood of the apex.

In the diastolic murmur of mitral stenosis a short interval often exists between the second sound and the murmur. This is rarely the case in aortic regurgitation, the murmur being continuous with or taking the place of the second sound. A slapping first sound with enlargement of the right heart with a gallop rhythm and a small pulse commonly indicates the presence of mitral stenosis, even though no murmur is heard.

In aortic regurgitation the apex-beat has a much more prolonged and exaggerated appearance, whereas that of mitral stenosis recedes almost instantly.

A thrill, if present, is of decided value. Yet with the Austin Flint murmur which may accompany aortic regurgitation a thrill is sometimes present, and these are the difficult cases, because it is here that the question arises not so much as to whether one valve disease or the other is present, but as to whether more than one valve is involved. In aortic regurgitation marked hypertrophy is present, whereas in mitral stenosis, if uncomplicated, none is demonstrable either by percussion or by *x*-ray. When, however, mitral regurgitation is present with mitral stenosis there is considerable hypertrophy, but not nearly as much as in aortic regurgitation.

It may be argued that in the early stage of aortic regurgitation there is little hypertrophy, but in nearly every instance when the patient presents himself for examination marked hypertrophy is present. It is, however, on the basis of signs outside of the heart that one must make the differentiation between these two simple lesions.

A previous history of syphilis or a positive Wassermann will almost clinch the diagnosis in favor of aortic regurgitation; on the other hand, a history of *rheumatic* fever inclines one to decide in favor of mitral stenosis. Yet it is not very rare to find aortic regurgitation due to rheumatic fever.

In mitral stenosis pulsation of the vessels is not common; in aortic regurgitation it is seldom or never absent. A marked Corrigan pulse is never observed in mitral stenosis. Duroziez's sign and the capillary pulsation of aortic regurgitation is also of decided value in excluding mitral stenosis. A loud systolic snap, the pistol-shot sound, in the large arteries, is often present in aortic regurgitation.

Blood-pressure.—In mitral stenosis there is not more than 50 mm. difference between the pressure in the arm and in the leg, whereas in aortic regurgitation this difference is between 60 and 120.

This rule is, of course, not universal, because in some cases of mitral stenosis associated with arteriosclerosis a greater difference than 50 may be recorded, but it is nevertheless a good working rule.

Pulse-pressure.—Ordinarily the pulse-pressure in mitral stenosis is a little below normal, whereas in aortic regurgitation it is nearly always double the normal.

Graham Steele Murmur.—In a small proportion of cases of mitral stenosis, one hears, in the third and fourth interspaces, to the left of the sternum, a soft blowing diastolic murmur as described by Graham Steele and named after him. It does not replace the second sound, but follows it after a short interval. It is sometimes heard all along the sternum.

As far as can be determined it is due to dilatation of the right ventricle with consequent functional insufficiency of the pulmonic valves. It is best heard when the patient is lying on his back; sometimes it is not heard when he is in an erect position; or again it may be heard only when he is in this position. It may or may not be affected by either inspiration or expiration. Exercise usually intensifies the murmur, which is best heard at that time. Pressure by the stethoscope sometimes renders it audible. It is not transmitted for more than an inch. Thus we have a secondary diastolic murmur in mitral stenosis just as we have a secondary murmur in aortic regurgitation, in the form of the Austin Flint murmur—two strong names for two weak murmurs.

As has been stated above, the murmur of pulmonary regurgitation is to all intents and purposes similar to and indistinguishable from that of the Graham Steele murmur.

Tricuspid Stenosis.—The murmur of tricuspid stenosis may be either presystolic or diastolic. The character of the murmur is just the same in tricuspid stenosis as it is in mitral stenosis. However, the murmur of tricuspid stenosis is usually heard only over the tricuspid area to the right of the sternum, whereas the murmur of mitral stenosis is commonly confined to the region of the left nipple.

Tricuspid stenosis is usually accompanied by a mitral stenosis. MacKenzie believes that we may make a diagnosis of tricuspid stenosis when pulsation of the liver, as determined by means of the sphygmographic tracing in the cardiogram, is found to be of the auricular type.

The early appearance of marked cyanosis and extensive edema is evidence in favor of the predominance of tricuspid stenosis as compared with mitral stenosis.

Austin Flint Murmur.—The presence of the Austin Flint murmur may raise the question as to whether true mitral stenosis is present in addition to aortic regurgitation or whether we have aortic regurgitation with a functional mitral stenosis due to ventricular dilatation. The Austin Flint murmur is not harsh and vibratory, as is that of mitral stenosis, and if a thrill is present it is not purring in character. In uncomplicated mitral stenosis the apex is in the normal position, whereas when the Austin Flint murmur is present the apex is displaced far to the left because of the enlargement of the left ventricle consequent on the aortic regurgitation.

The Austin Flint murmur is, of course, heard in the same location as the murmur of mitral stenosis. In fact, the most satisfactory explanation of its origin is that there is a relative functional mitral stenosis, produced by the dilatation of the ventricle, so that, given a diastolic murmur at or about the nipple, the presence or absence of aortic disease and its concomitant symptoms will determine the diagnosis.

The sound due to an adherent pericardium seldom causes trouble in diagnosis. This is particularly true in children. This sound is rather a rumble than a murmur, and is best heard in diastole at the apex. It does not have the same sharply defined localization as does the murmur of mitral stenosis, and the peculiar slapping first sound of mitral stenosis is not present.

Combined Murmurs.—When the question arises as to whether or not one is dealing with combined mitral disease, it may be well to remember that the murmur of aortic disease is frequently transmitted to the apex of the left ventricle and is not so well heard over the body of the right ventricle. In such a case one will hear the systolic or diastolic murmur of aortic disease down to and to the left of the apex, but not to the right of the apex. In such a case the hypertrophy is very much more marked than in ordinary disease; furthermore, the apex-beat is much more thumpy in character, as felt under the hand, and, finally, the diagnosis must frequently be made on the basis of signs outside of the heart, as mentioned above. It is very uncommon that the murmurs of mitral disease are transmitted to the base, but when such is the case the final judgment may again be based on the peripheral signs outside of the heart. When combined lesions of both orifices are present, the murmurs are most clearly heard over the ordinary points of greatest intensity; then they gradually fade as one goes from either apex to base, and gradually increase as apex or base is approached. In solving such problems, one should select one murmur and follow it throughout its course, and then do the same with the others. In the rheumatic cases in children basal and apical involvements are quite common.

In more than one-half of all patients suffering from cardiac disease, a combination of murmurs is present sooner or later.

In the table of F. J. Smith the relative frequency of combinations of murmurs found is given as follows:

A. R. and M. S.	16.55 per cent.
A. S. and M. S.	6.12 per cent.
A. R. and M. S.	5.21 per cent.
A. R., A. S., M. S. and M., presystolic	3.77 per cent.

Often these combined murmurs are due rather to relative insufficiency than to true organic change, which is often an effort on the part of nature to prevent serious consequences. For instance, in aortic regurgitation the relative insufficiency of the mitral valve prevents an overdistention.

In advanced mitral disease a marked leakage at the tricuspid valve likewise prevents overdistention of the right heart.

It is only when mitral regurgitation is secondary to aortic stenosis that combinations are apt to be serious in themselves. Aside from this, it is a well-known fact that patients suffering from disease of both mitral and aortic orifices are more prone to develop malignant endocarditis than is the case when either valve alone is affected.

A common difficulty in defferentiating murmurs is to determine whether the murmur heard at the base and the one at the apex are due to involvement of one or of both orifices. When the disease at the orifice has persisted for some time, whether it is regurgitation or stenosis, there is nearly always, sooner or later, a concomitant stenosis or regurgitation. If we are dealing primarily with a mitral stenosis which is moderately advanced, there will also be some regurgitation, and the same thing applies with regard to stenosis when regurgitation is the primary lesion. When mitral stenosis and mitral regurgitation are both present there is a possibility of mistaking the seesaw murmur for a prolonged systolic murmur. At another examination, however, we are likely to find a systolic murmur, and the absence of a second sound at the apex justifies the diagnosis of stenosis.

When mitral regurgitation accompanies mitral stenosis, the palpatory signs so marked in uncomplicated stenosis are often not so clear. The presence of the Austin Flint murmur, *i.e.*, a presystolic murmur at the apex present in aortic regurgitation, may be confusing, inasmuch as a thrill is present here as well as in mitral stenosis; but in the Austin Flint murmur there is a strong, long first sound and a much hypertrophied heart, whereas, in mitral stenosis, the first sound is snappy, the heart is not enlarged, and there is an accentuated pulmonic sound.

The individual symptoms are seldom pathognomonic in themselves, because in one instance, a symptom which is usually present to a marked degree in mitral disease may be very pronounced in aortic dissease, and *vice versa;* but the ensemble of symptoms is essentially different. Mitral stenosis, in its early stages, commonly manifests itself by lung signs, as dyspnea, cough, and hemorrhage, whereas aortic disease is manifested, in its early stage, by pressure disturbances such as headache, throbbing, and pain over the heart; dropsy and enlarged liver are, relatively speaking, early signs in failing mitral disease; if they appear at all in aortic disease, it is toward the end. Ordinarily the appearance of either the mitral facies, a history of rheumatic fever, cerebral embolism or fibrillation point to mitral stenosis, rather than to aortic disease.

The presence of hemorrhagic expectoration commonly raises the diagnostic question of the coëxistence of tuberculosis. In fact, mitral disease is more commonly mistaken for tuberculosis than for anything else.

The added presence of a slight rise in temperature due to fresh infection of the valves or to an acute bronchitis, the flushed face, dyspnea, and cough, would seem to make a complete picture of tuberculosis, were it not for the absence of the bacillus of Koch. Yet clinical experience the world over shows that the two diseases are seldom actively present together in the same individual. Every now and then some competent observers come forth with statistics proving that in a series of autopsies the diseases were concurrent, but one or the other of the lesions is always in a quiescent form.

Sears goes so far as to state that 1 per cent. of the cases of mitral stenosis at the Boston City Hospital were presumably tuberculosis; yet close analysis will show that in comparatively few cases could the fatal issue be charged up to a combination of the two active lesions.

If every one is tuberculous, then every patient with cardiac involvement must also be tuberculous, but progressive pulmonary disease in mitral stenosis is the exception. This immunity has been explained on the ground that mitral stenosis promotes pulmonary hyperemia, and it is a well-established fact that hyperemia is the best antagonist against the growth or propagation of the organism of tuberculosis.

In rare cases cardiac thrombosis causes the symptoms as well as many of the physical signs of mitral stenosis. The onset is sudden with great dyspnea, cough, rapid feeble pulse and later, in some instances, a localized gangrene of the foot. The reason for this latter phenomenon is not quite clear. In addition, there is usually a murmur, presystolic in time, and a reduplicative second sound. However, the rapid onset and the previous history are usually sufficient to justify the diagnosis.

Complications and Sequelæ.—In approximately 75 per cent. of the cases of true mitral stenosis there is sooner or later an added regurgitation.

Thrombosis of the left auricle, for reasons to be pointed out under Pathology, is more common than in any other valvular lesion. It cannot be diagnosticated except when the thrombus has been loosened from its bed, and thus furnishes emboli. Embolism of the left mid-cerebral artery is the most common clinical manifestation met with. The consequent right-sided paralysis and speech defect are seldom overcome, and while the condition has a low immediate mortality, it has the worst outlook as to complete recovery of function. If one can exclude syphilis, it is the most frequent cause of hemiplegia in patients under forty years of age. It may sometimes be diagnosticated by a sudden rapid rise in temperature immediately following a hemiplegia when there is no other explanation for the temperature. Of course,the customary rise in temperature which occurs antemortem in most fatal hemiplegias is of no diagnostic value.

Splenic infarcts are probably still more common, but are usually symptomless. Many of the sudden pains complained of by cardiac patients in the lower left side are doubtless due to this same cause, but one cannot be certain of their differentiation.

Pulmonary emboli in cardiac patients arise either from the thrombi occurring in the veins throughout the body or from those arising on the right side of the heart, or more commonly, from clots emanating from the left auricle as mentioned above and reaching the lungs through the greater circulation.

Pulmonary thrombosis is sometimes due to stasis in the pulmonary circulation, thus producing clots in the pulmonary artery.

Infarction, as a result of such obstruction, is fairly common in the latter days of the life of the cardiac patient, but it is neither as dramatic nor as terrifying as when it comes from the left side of the heart.

Pulmonary embolism explains some of the attacks of *hemoptysis.* In others, localized pneumonic areas are responsible for the bleeding. About 20 per cent. of all the cases of mitral stenosis show hemoptysis at some time during their course. It is rarely alarming, and usually the patient feels better after the hemorrhage. Profuse bleeding, however, offers a grave outlook. It often follows emotion or strong effort of any kind. On the other hand, blood-stained mucus is quite commonly expectorated by the majority of patients suffering from dilatation of the right heart due to any cause.

Hemorrhage from the nose is particularly common in children. When it is profuse it greatly depresses the child and hinders recovery. It should be considered a serious complication.

Hemorrhage from the stomach occasionally occurs, and has a greater significance than any other hemorrhagic manifestation.

Hemorrhage from the uterus is not uncommon, but does not seriously affect the patient unless it is very profuse.

Hysterical manifestations are much more common in young women suffering from mitral stenosis than in those suffering from any other valve lesion. They frequently suffer from attacks of dyspnea, palpitation, and even pain closely resembling that in angina pectoris, and much care must be exercised in not laying too much stress on their complaints, thereby causing undue alarm.

The nervous element outweighs the organic, as a rule, and the patient is not in as serious a condition as she appears to be. Such attacks are most common at the menstrual period. Attacks of migraine are also more common than in normal patients.

Auricular fibrillation may be considered a symptom rather than a complication of mitral stenosis, for it is more often present in this form

of valvular disease than in any other. In some instances it begins suddenly and is continuous thereafter; in other cases the irregularity persists for a short time, then disappears and reappears at intervals until it becomes continuous.

In some patients attacks of paroxysmal tachycardia take its place, and this is not to be wondered at, since these two functional disturbances are closely allied, and seem to represent a difference in degree of hyperexcitability rather than a difference in origin.

Venous thrombosis in other parts of the body is more common in mitral stenosis than in the course of any other valvular lesion.

Enlargement of the liver is more common as a consequence of mitral stenosis than following any of the other principal primary cardiac lesions. Ascites likewise arises earlier than in other heart lesions, and persists longer. The reverse is true for mitral regurgitation. Mitral stenosis is often associated with a small kidney. In fact, this association is so common that these conditions appear to have a common infectious origin.

Adherent pericardium is fairly common in children, and some form of pericarditis is present in one-third of all the fatal cases of mitral stenosis.

PREGNANCY.—Mitral stenosis is the most serious valvular lesion associated with a pregnancy. The principal immediate danger is the sudden development of pulmonary edema. However, until there is a decided break in compensation there is comparatively little danger. Many women with compensating mitral stenosis pass through half a dozen pregnancies with no evil effects. If there has been any disturbance in compensation the child is not so likely to live as in normal cases. From 25 to 40 per cent. of such patients have premature labors. As a rule labor itself is well borne, even in uncompensated cases.

Prognosis.—Next to aortic regurgitation, mitral stenosis is the most serious form of valvular lesion. According to Broadbent's statistics, the average age of death is from thirty to thirty-nine years for males and from forty to forty-nine for females. These statistics represent conditions in London, and are not applicable to the cases seen in civil practice in this country.

The reason for the greater seriousness of mitral stenosis as compared with mitral regurgitation, is that the consequences of the obstruction are not so easily overcome.

Mitral stenosis is a disease of youth, and there is more tendency to contraction at that time than later in life; furthermore, the size of the orifice, as a result of the contraction, does not increase, whereas the cavities of the heart will continue to increase as the heart normally grows larger. Thus we find in adult life a normal-sized heart with a mitral orifice the size of that in a child's heart.

Broadbent's four stages form a convenient way of fixing in one's mind the progress of the disease from the standpoint of physical signs as well as of prognosis:

First Stage.—*Presystolic Murmur.*—Slapping first sound and second sound well heard at the apex, and the accentuation of same over the pulmonic area. The compensation being good, the prognosis is favorable at this time, and the patient is not a source of concern.

Second Stage. — *Presystolic Murmur.* — Thrill and first slapping sound present, but the second almost inaudible at the apex. (Students generally confuse the sounds, and are apt to mistake the first sound for the second.)

Third Stage.—Presystolic murmur and thrill have disappeared, as well as the second sound at the apex. There is a short, sharp first sound. Auricular fibrillation is present. The signs of beginning broken compensation, such as shortness of breath, cough and hemoptysis, are now present. This condition may exist for many years.

Fourth Stage.—Broken compensation and stasis; later on signs of tricuspid insufficiency, venous pulse, and pulsation of the liver.

To sum up, as long as the second sound can be heard about the apex there is no immediate danger. When the second is lost at the apex the patient is fairly safe, provided there are no infections, and that the patient does not indulge in excitement or exertion. But there is no reserve force, and the least disturbance is sufficient to induce a break in compensation, so that, to use a slang expression, the patient must constantly "walk the chalk line." This may be impressed upon him better if it is explained that he is like a man walking along the edge of a precipice—he may do so indefinitely, but if the slightest wind strikes him, or the slightest misstep occurs, he will almost certainly fall over; whereas another man (representing one with a sound heart) walking along the same table but several feet from the edge may be struck by the same wind-storm and yet will not fall over the edge. Some such homely expression as this brings his condition vividly to the mind of the patient, and serves to warn better than hours of preaching. Such patients often live a quiet life for many years, but they are in constant danger.

The third group are those with serious symptoms, such as edema, and dyspnea. Here one must judge how severe or how slight the causes are that have brought on the break in compensation.

The reason why women live longer than men is because they usually live a more quiet life. Once a severe break in compensation occurs recovery is not nearly as easy or as frequent as in mitral regurgitation. Among females the greatest single danger lies in pregnancy. No other lesion is so serious to the pregnant woman as mitral stenosis, yet sometimes it has very little effect, some patients going through as many as nineteen pregnancies with no evil results. It is not regarded as seriously as it was in former years. The chief danger is during the fifth and sixth months, and then the calamity generally occurs in the form of acute pulmonary edema. Death from pulmonary edema rarely occurs during labor, but it is usually within two hours after labor that pulmonary edema manifests itself.

If there have been no breaks in compensation, however, previous to pregnancy, these patients generally do as well as other women who have no such lesion; lactation does not affect them seriously.

When the presystolic murmur disappears and the diastolic takes its place the disease has advanced considerably. Children, of course, have a less favorable outlook than adults. When mitral stenosis is associated with, or due to arteriosclerosis, the outlook is much less favorable than otherwise.

There is a class of patients who present evidence of rheumatic mitral disease without having a history of rheumatic fever. These patients absolutely deny having had articular rheumatism. Generally they give a history of backaches, and of sticking pains in the muscles and in the finger-joints, which they have usually associated with their work.

There is no history of rheumatic fever in childhood, nor any of the severe infectious diseases which are commonly followed by rheumatic fever, yet the heart presents the murmur of mitral stenosis. When there is a break in compensation in these cases they do not do as well as those with a frank rheumatic history. This type is especially common among the Russian Hebrews. The outlook for eventual recovery among those patients is seldom promising.

Of all diseases of the heart, mitral stenosis is most commonly associated with auricular fibrillation. In Carey Coomb's statistics the average age of the onset of this symptom is twenty-six years, and the average expectation of life after that is thirteen years; he believes that most of the cases have their origin in mitral disease before the age of sixteen.

Cerebral embolism is by no means uncommon. The patient rarely recovers completely from the hemiplegia which results, in contradistinction to hemiplegia of cerebral hemorrhage. It is usually a right-sided hemiplegia. Most patients, however, die from gradual heart-failure. There is engorgement of the lungs, bronchitis, edema, pneumonia and death. In estimating the course of heart-failure one must analyse:

1. The course of the symptoms of insufficiency, *i.e.*, pulmonary congestion, dyspnea or exertion, the presence of congestion at the left base, and liver enlargement.
2. The auricular fibrillation. The length of life after this is established varies from five to fifteen years.
3. The failure of the ventricle. When this happens, there is intense hyperemia of the lungs. Following this there is frequent hemoptysis Sometimes this is followed by pronounced relief, but in any case in which it is quite profuse it is a warning of the near approach of death. In such cases, when vomiting becomes persistent, recovery is uncommon. As far as treatment is concerned, the prognosis depends upon how soon the patient is put to bed and given digitalis. When both of these measures are pushed to the limit, *i.e.*, absolute rest, achieved if necessary by the use of opium, and large doses of digitalis, and these measures fail to slow the pulse and lessen the symptoms within ten days, the outlook is very grave.

MODE OF DEATH.—Very often death follows an intercurrent affection. The ordinary patient suffering from progressive mitral stenosis usually dies in bed as a consequence of the progressive edema, anasarca and hydrothorax. Even though the patient is bedridden the end usually comes quite unexpectedly. He is apparently no worse than he has been for days or weeks, or is possibly a little better, when out of a clear sky, during the late hours of the night, an attack of pulmonary edema develops and death closes the scene, or again, the cheerful patient asks for a drink, takes it, thanks the nurse, turns over, and is dead. In this sense sudden death is not uncommon. In the case of those who are up and about and free from marked symptoms, not more than 2 per cent. suffering from this lesion die suddenly.

Pathology and Pathological Physiology.—There are three varieties of the lesion presenting different pictures, depending upon the causes: (1) infectious, (2) arteriosclerotic, (3) congenital.

Of these the first is by far the most common. In addition, one sometimes finds a functional form such as results in the production of the Austin Flint murmur in aortic regurgitation; in this case there is no pathologic change in the mitral valves themselves, but the relative constriction is due to a retroversion of the valves due to the dilatation of the ventricle consequent on aortic regurgitation. However, thus far this is only a theoretical surmise.

There is a rare form due to a congenital lesion; it may also be a result of a fetal endocarditis. This congenital variety is commonly found in association with other congenital defects in patients suffering from hare-lip, cleft palate, etc. Probably a large number of the cases described under this head are due to unrecognized early endocarditis, sometimes becoming manifest between the seventh and fourteenth year of life.

The fact that such patients live longer than those who acquire the disease later on in life may be due to their early recognition of the limitation of activities in the different forms of infection. Hereditary syphilis may be an occasional cause of the infection in these early cases.

A primary lesion and a secondary form are associated with mitral regurgitation. The latter is more common than the former, but because of the accompanying regurgitation it does not produce a definite pathological picture.

Anatomically one meets with four varieties of lesions in mitral stenosis: buttonhole, funnel-shaped, vegetative and, very rarely, cystic.

When the lesion involves the free edges of the valve a funnel-shaped orifice is formed, the mouth of the funnel being situated at the ring, and the small end of the funnel being drawn down toward the apex by the shortening of the chordæ tendineæ and of the papillary muscles, the valve-tissue itself forming the sides of the funnel.

This is the usual type seen early in life, and may be described as the typical infectious type.

Later in life the button-hole variety is more common. This is frequently due to added arteriosclerosis. It is associated with a thickening or shortening of the papillary muscles and chordæ tendineæ. The valve itself does not stretch, as in the early cases, but becomes much thickened, and there is a great increase of fibrous tissue, which leads to puckering of the valves. Often the leaflets unite and form a diaphragm which is perforated by a slit-like opening. This union of the cusps almost entirely closes the orifice and presents the appearance of a buttonhole when looked at from above; hence the name. The vegetative form is similar to that described under mitral regurgitation; the cystic form is rare and resembles the vegetative type.

In the heart two forms of thrombi are met with postmortem: One is the infectious type which occurs as the result of endocarditis; these are small, and are generally found on the valve edges. The other form is usually found in decompensating hearts, and is met with in those portions of the heart in which the current of blood is less active and in which there are uneven areas. These conditions are to be found particularly in the appendages of the auricles and to a lesser degree between the columnæ carneæ at the apex of the ventricle. They are much larger than those in the infectious form. Ball thrombi are a special form met with in the left auricle in mitral stenosis.

According to Norris the mitral orifice in men averages 110.37 mm. and in women 92.68 mm. in circumference. The anterior mitral leaflet has a different function from that of the small, fixed, posterior leaflet. The anterior leaflet, in addition to preventing regurgitation in the auricle during the systole of the ventricle, actually forms, together with the septum of the ventricle, a channel which aids in conducting the contents of the ventricle into the aorta, so that the pathology in this cusp is more significant than when it is present in the posterior one.

The earliest effect of mitral stenosis is a hypertrophy of the left auricle; because of the slow output the left auricle becomes extremely full, and forces a large amount of blood into the ventricle. As it continues to distend it finally reaches a point at which dilatation ensues. This dilatation makes itself evident at first in the auricular appendage, because, owing to the unyielding structures with which the auricle is surrounded, there is little chance for this chamber to increase by stretching. Because of this dilatation of the appendix one finds thrombosis in the appendix, either antemortem or postmortem, with great regularity. As a result, this space is a reservoir, as it were, for emboli, and makes for less efficiency in the presence of any strain or infection.

Finally, as a result of venous stasis, the right ventricle hypertrophies and becomes rectangular in shape. After this, dilatation of the ventricle occurs because of the continuous pressure, and tricuspid insufficiency results. Later on this is followed by overdistention of the right auricle. It gradually becomes thinned out, and is nothing more than a funnel-like continuation of the vena cava; thus the functional activity of the auricle is destroyed, and to all intents and purposes it does not exist. This phenomenon can be demonstrated by the disappearance of the auricular wave in the jugular tracing during auricular fibrillation. While this sequence of events takes place to some degree in all cases, it can never be sufficiently emphasized that it does not take place as long as the muscle of the heart is perfectly sound, or in other words, as long as there is sufficient ''rubber'' in it to make up for the valve deficiency. It is only when valve and muscle are sufficiently involved by pathological changes that this sequence follows.

As was pointed out earlier, the left auricle can expand only in an upward direction. This expansion upward may result in pressure on the left pulmonary artery, and in that way produce a paralysis of the left recurrent laryngeal nerve by pinching it between the pulmonary artery and the arch of the aorta.

When left ventricular hypertrophy is present it is usually due to other lesions and not to mitral stenosis.

Experimentally, McCallum and others have produced mitral stenosis by introducing a distensible balloon through the auricular appendage and by clamping the auriculoventricular ring. The immediate result of this procedure is the lowering of general arterial pressure throughout the body, and the elevation of pressure in the pulmonary artery, pulmonary veins, and left auricle. The pressure in systemic veins is little elevated. The essential features of this experiment are that the amount of blood in actual circulation is diminished while the rest of the blood stagnates behind the obstruction into the lungs. Such rapid changes, however, do not take place in the hearts of human beings suffering from mitral stenosis.

TRICUSPID REGURGITATION

Etiology.—There are two classes of cases, if one expects the rare congenital cases which are associated with tricuspid stenosis:

1. Those due to a primary lesion of the valve, such as follows acute endocarditis, with resulting fibrosis. This is an extremely uncommon type.

2. Instances of relative incompetence wherein the valves are normal and the dilatation is due, as in mitral regurgitation of the same type, to the dilatation of the right ventricle. In these dilated hearts the normal leaflets are no longer able to close the increased abnormal orifice. This relative incompetence is the most common cardiac lesion and is present in practically all cases of cardiac failure at some time or another. It is always consequent on some other disease. Etiologically it occurs most frequently (1) secondary to valvular diseases of the left side of the heart, particularly the mitral lesions; (2) acute and chronic myocardial involvement, due to infection, toxemia or degeneration; (3) pleuro-pulmonary diseases associated with increased pressure in the pulmonary circulation, as in emphysema, cirrhosis of the lungs and adhesive pleurisy, or (4) the temporary dilatation and over-strain of the right

ventricle, due to any unusual or sudden physical exertion, the "safety-valve action" of Wilkinson King.

Osler calls attention to the fact that one may imitate tricuspid functional incompetency by holding the breath for one minute; as a result of this the right border of the heart extends to the right of the normal at least an inch further than before. This may be determined by deep percussion or by *x*-ray examination.

Symptomatology.—The symptoms have been described under Mitral Regurgitation, which is so commonly the diagnosis in the first instance.

PHYSICAL SIGNS.—*Inspection.*—The face and extremities are cyanotic; the veins show a distinct pulsation. There is also epigastric pulsation. When the disease has developed slowly, or in young people, the precordium is distinctly bulging. The retraction of the third and fourth interspaces between the sternum and parasternal line is quite marked.

Palpation.—When the condition is well advanced, a systolic pulsation is frequently felt over the right ventricle. The apex is diffuse; its location depends upon the primary disease. If mitral regurgitation is present it is usually displaced beyond the nipple line. If early mitral stenosis is the cause, it is within the nipple line.

The liver pulsation, when present, is pathognomonic. To determine this sign the patient should lie with his arms extended above his head, with the palm of the physician's left hand over the right mid-axillary region, and his right hand over the upper abdominal region. An expansible pulsation of the liver, synchronous with the systole of the heart, will be felt, if this disease is present.

In well-advanced cases the venous pulse, instead of being diastolic in time, is systolic, the positive venous pulse of Siegel. This is due to the fact that the auricle, in decompensated hearts, is to all intents and purposes a continuation of the vena cava, so that, when systole of the right ventricle occurs, the blood is forced in two directions: (1) into the pulmonary artery, and (2) up into the vessels of the neck. In the earlier stages of the disease this does not occur. The jugular tracing is quite characteristic, the "ventricular type" of Mackenzie.

Percussion.—Cardiac dulness extends to the right of the sternum and is often as much as two or three inches beyond the midsternal line.

Sometimes the relative tricuspid insufficiency produces a wider area of dulness than does that due to organic lesion, but the percussion findings are more permanent in the organic lesions. The murmur takes the place of the first sound and is heard throughout the whole systolic period. It is a systolic murmur and is best heard on the left side very near the sternum in the fourth and fifth interspaces, or at the base of the ensiform cartilage. Very frequently it is best heard on the right side of the sternum. It is transmitted downward along the sternum, but not to the apex. It gives one the impression of being superficial or near the ear. It is a very fugacious murmur. Sometimes in the course of an examination it is present only during a few beats. It is more marked after exertion and in certain postures of the body.

Hirschfelder suggests that it may be elicited by causing the patient to bend forward at an angle of 45 degrees occasionally. Sometimes it is best heard when the patient's head is lying over the edge of the bed, thus putting the vessels under a tension. The physician then listens over the tricuspid region.

In spite of all these maneuvers, it is frequently very difficult to elicit a murmur, even though one is quite certain that tricuspid regurgitation is present. The murmur is generally faint or absent when there is a large leakage due to severe insufficiency; on the other hand, slight regurgitation generally produces distinct murmurs.

Differential Diagnosis.—The principal difficulty in the diagnosis is differentiating between mitral regurgitation and *tricuspid regurgitation.* The murmur occurs at the same time in both, and the mitral murmur is frequently transmitted over a large area of the heart.

The difference is largely an academic one, because sooner or later, mitral disease is followed by tricuspid regurgitation. In practice, the diagnosis of tricuspid disease is founded upon the presence of symptoms rather than upon physical signs.

In tricuspid disease the murmur is not as rough as the mitral form. It is more superficial and is higher-pitched. The mitral murmur is rarely heard over the right side of the sternum.

In tricuspid disease the pulsations are visible over the right border of the heart, whereas in the mitral regurgitation they are visible to the left.

In differentiating the murmurs it is well to remember that the mitral systolic murmur has its point of maximum intensity somewhere near the nipple and gradually diminishes in intensity as one passes toward the right. On the other hand, the murmur of tricuspid disease has its greatest intensity at the left sternal border, and it also diminishes as one advances to the left, so that there is an area between these two regions in which the sounds are faintly heard. The diagnosis must generally be based, however, upon the presence of the jugular and hepatic pulsation, dropsy and cyanosis.

Sometimes the question arises as to whether the disease is organic or functional. In general the organic murmurs are rough, while those resulting from functional insufficiency are soft and blowing.

In organic insufficiency, after compensation has been reëstablished, the positive venous pulse still remains. In relative insufficiency under the same conditions the positive venous pulse changes, so that the auricular wave again becomes prominent.

Prognosis.—The prognosis depends upon the primary cause. In those cases secondary to mitral stenosis due to relative insufficiency, the immediate outlook in the early attacks of decompensation is favorable. In general the outlook has already been described under Mitral Regurgitation and Mitral Stenosis.

In aortic disease, the presence of tricuspid insufficiency is the beginning of the end. In primary organic disease of the tricuspid orifice the progress is usually steadily downward.

Pathology and Pathological Physiology.—In the organic cases the lesions are the same as those found in mitral disease only, of course, situated in the right heart. When the regurgitation in the cases of relative insufficiency is very marked, the dilatation of the right auricle is the first and most characteristic gross lesion.

In the organic cases both auricle and ventricle are hypertrophied as well, because here the condition has been of longer duration and more gradual in appearance. The chief effect of this is evident upon the systemic veins; the back flow of blood causes the venous pressure to [illegible] (20 mm. of Hg). This causes stasis and is followed by dropsy. In cases which have existed for a long time, or in which there have [illegible] frequent attacks of broken compensation, the congestion in the [illegible] frequently results in the production of "nutmeg liver."

TRICUSPID STENOSIS

Etiology.—This is a comparatively rare lesion. In a total of 12,000 autopsies at Guy's Hospital, covering a period of twenty-six years, only 87 cases were found. Among 24,000 cases admitted to Johns Hopkins Hospital, the condition was found only 7 times, and then always combined with other lesions. About one-third of the cases are congenital in origin and then the disease is usually associated with some other abnormality.

The acquired form is due to a previous attack of endocarditis. It is then almost always associated with mitral stenosis. The statistics show that females are affected three times as often as males.

Symptomatology.—Cyanosis is the first symptom to attract attention, and is the most characteristic of the early manifestations. It frequently precedes all other symptoms by a year or more. In no other disease of the heart, with the exception of a congenital defect, is cyanosis such an early symptom. These patients complain bitterly of cold on the slightest exposure. Later, extreme dyspnea is present, following slight exertion, and is the chief complaint. Inasmuch as mitral stenosis accompanies the lesion in such a large proportion of cases, the symptomatology is in general similar to that of mitral stenosis. Polycythemia and clubbed fingers are generally present when the lesion is discovered.

Anasarca is a comparatively early symptom. Pulmonary congestion with prune-juice sputum is frequent. Sudden death is fairly common. Later on the symptoms of tricuspid regurgitation, such as edema, enlargement of the liver, etc., are added.

Diagnosis.—Physical Signs.—The disease is rarely recognized during life. When discovered it is usually in combination with mitral stenosis. The area of heart dulness is increased to the right. This is due to the dilatation of the right auricle.

Sometimes there is a presystolic thrill and snapping first sounds similar to those of mitral stenosis.

There is a short presystolic murmur just to the right of the sternum in the fifth intercostal space. Sometimes it is only heard over the lower sternum. The murmur of mitral stenosis, which is so commonly associated with this condition, is usually only heard over a limited area about the left nipple, and the sound grows fainter as the sternum is approached. The tricuspid murmur, on the other hand, becomes more pronounced as one approaches the mid-sternum region.

Liver pulsation occurs relatively early, and with a polygraph it can be demonstrated that this pulsation is auricular or presystolic in time. The same holds true of the jugular pulsation. Commonly the distention of the jugular veins is without visible pulsation, and without the polygraph it cannot be determined.

Differential Diagnosis.—The only serious question consists in the differentiation between mitral stenosis and tricuspid stenosis as both are commonly present when mitral stenosis can be demonstrated. The problem is only difficult when a presystolic or a diastolic murmur of mitral stenosis is present, and transmitted to or beyond the sternum. One must then make the diagnosis on the basis of the concomitant symptoms. In tricuspid stenosis, cyanosis is a relatively early, marked and continuous symptom, whereas it is a late symptom in mitral stenosis. Dropsy is an early symptom in tricuspid stenosis and appears late in mitral stenosis. The evidence of the polygraphic tracing may occasionally be of help, but after all, comparatively few practitioners have the time or instruments to devote to such an examination. When the murmur in rare cases has become mid-diastolic in time, it is occasionally confused with aortic regurgitation, the murmur of which is sometimes heard in the same area. The other evidences of aortic regurgitation are sufficient to prevent a mistaken diagnosis.

In a failing mitral stenosis a systolic venous pulsation, if present, is due to tricuspid regurgitation, and each time that the right ventricle contracts there is a systolic pulsation in the veins of the neck, whereas in tricuspid stenosis the pulsation occurs just before systole, and is due to a contraction of the auricle and not of the ventricle.

The diagnosis is seldom made during life, and is only possible if a complete clinical picture is present. This consists of a cyanosis of long duration, increased size of the right auricle as demonstrated by x-ray and by percussion, a presystolic thrill and murmur over the right sternum region, liver pulsation, and a sphygmographic tracing.

Prognosis.—In Pitt's series quoted by Osler, of 87 patients 31 died between the ages of twenty and thirty years.

Malignant endocarditis affects the tricuspid valve oftener than does the benign form of endocarditis.

The outlook usually depends upon the severity of the associated mitral lesion and upon the muscle on the left side of the heart. When this begins to fail the course is steadily downward. Compensated tricuspid stenosis may exist for several years, with several breaks in compensation; but this is not the rule. When dropsy sets in, unless it disappears promptly under rest it will probably not respond to any treatment. Sudden death is fairly frequent.

Pathology and Pathological Physiology.—The changes found in the valve are identical with those found in mitral stenosis. In old cases, cirrhosis of the liver, and perihepatitis are frequently found. The pathological physiology is the same as that of mitral stenosis with the difference that the systemic veins are affected instead of the pulmonary veins.

When narrowing goes on to such an extent that the auricle does not entirely empty itself, then the contraction of the muscle of the auricle drives the blood back into the vena cava, and thus slows the circulation in the heart and lungs. As a result of this slowing the oxygenation of the blood is lessened, and cyanosis occurs. As a consequence of this cyanosis, polycythemia appears.

After the hypertrophy of the auricle becomes extreme, dilatation follows, and the contraction of the auricle can no longer be made out in the polygram as a presystolic wave. After this, no further compensation can take place, and the slightest strain or infection produces dropsy and enlarged liver.

PULMONARY STENOSIS

Etiology.—Pulmonary stenosis is almost always a congenital lesion, and, as such, constitutes a fairly large percentage of what is, comparatively speaking, a very rare condition, *i.e.*, congenital heart disease. As an acquired lesion it is extremely rare. The causes are the same as those of the stenosis of the other valves. Of these, endocarditis is the most common.

Symptomatology.—In the acquired form there are no marked symptoms until there is some loss in compensation. In the congenital cases, of course, cyanosis is an early and consistent symptom, and is associated with clubbed fingers. With loss of compensation, dyspnea, dropsy and cyanosis are in evidence and are commonly progressive.

Physical Signs.—*Inspection.*—Until there is loss in compensation, there are no distinct signs on inspection. Usually, however, when the case is first seen the picture of tricuspid regurgitation is already present.

Palpation.—A systolic thrill may be felt at the base in the second and third left intercostal spaces, just to the left of the sternum. There are no characteristic changes in the pulse until tricuspid insufficiency is added, when the picture of that disease becomes evident.

Percussion.—Dulness is increased to the right as a result of the hypertrophy of the right ventricle.

Auscultation.—The diagnosis is based upon the presence of a systolic murmur heard with maximum intensity close to the sternum in the second left intercostal space. It is transmitted upward and toward the left clavicle. It is a harsh murmur and lasts through the entire systole. It gives the impression of being closer to the ear than do the other murmurs. The second pulmonic sound is very faint, or, more often, cannot be heard at all.

Diagnosis.—As an acquired lesion it is an extreme rarity, and the diagnosis may seldom be established. On the other hand, the diagnosis of the congenital form may frequently be made. The frequency with which systolic murmurs are heard at the base of the heart renders it necessary to call attention again to their relative lack of diagnostic importance. Pulmonary stenosis is the rarest cause of this murmur. A bend in the pulmonary artery is one of the most frequent causes. Next to this, anemia is the most common factor. If true pulmonic stenosis is present, the second pulmonic sound is faint or absent.

The murmur of aortic stenosis is well heard in the same area, but is transmitted up unto the vessels of the neck. The second aortic sound is faint or absent, and there is left hypertrophy, plus the slow characteristic pulse.

Prognosis.—The patients with congenital disease seldom live many years. As long as those with acquired stenosis do not present symptoms they are only in potential danger. At the onset of any well-developed signs of decompensation the progress is rapidly downward. Pulmonary stenosis impedes the blood supply to the lung, and this produces a condition which is the reverse of mitral stenosis. As a consequence most patients who survive this disease for any length of time eventually die of pulmonary tuberculosis.

Pathology and Pathological Physiology.—The postmortem changes in the valve are similar to those in stenosis of the aortic valve. In some cases the conus of the right ventricle is involved. Generally speaking, vegetations, sclerosis, and calcareous deposits occur, as in the other valves. The obstruction of the outlet of the right ventricle increases its work, similar to that occurring in the left ventricle in aortic stenosis; consequently there is hypertrophy. The right side of the heart is not, however, constructed so that hypertrophy may go on indefinitely as is the case with the left side, so that within a short time it dilates. Tricuspid insufficiency follows, with all of the evidences of broken compensation.

PULMONARY REGURGITATION

Etiology.—This is an extremely rare lesion. Up to 1910 Norman Pitt was able to collect only 10 undoubted cases in the literature. It occurs as in the other forms of regurgitation, (1) as a result of endocarditis (of which the gonococcus has been the exciting cause in one-half of the recorded cases) or, (2) due to the inflammatory change associated with aneurysm of the aorta, (3) rarely, as a congenital lesion, or (4) as a relative insufficiency. This relative insufficiency follows or is associated with any great increase in pressure in the pulmonary artery. It is most commonly found in association with the disease producing this back-pressure, as in mitral stenosis and chronic emphysema. When it is associated with mitral stenosis it is thought by some to produce the Graham Steele murmur.

Symptomatology.—Unless there has been a break in compensation there are no distinctive signs of the disease. The most characteristic symptom is dyspnea, but dyspnea on exercise is such a common symptom in cardiac disease that it is in itself of little diagnostic value. In this disease it sometimes occurs in paroxysms without any evident cause. The slight cough which accompanies any pulmonary congestion is usually present in all of these cases.

Sepsis, particularly gonorrheal sepsis, has an affinity for this valve, and it should be examined in all cases of septicemia.

Physical Signs.—*Inspection.*—The associated lesion commonly masks most of the physical signs. On inspection cyanosis is sometimes found to be present. The evidences of the dilated right ventricle and conus arteriosus, as shown by the pulsation in the second and third interspaces, as well as in the epigastrium, are usually present.

Palpation.—When dilatation has taken place pulsation may be felt in these above-mentioned spaces. The diastolic thrill is rare. Dulness on percussion can be made out to the right of the sternum.

Auscultation.—The diastolic murmur is the most distinct sign of the disease. It is best heard at or near the left second costal cartilage. Occasionally it is best heard an inch or two below this point. It is not transmitted to any extent, and then only downward. It gives one the impression of being near the ear. Usually it is a soft, blowing murmur.

Differential Diagnosis.—The condition rarely presents diagnostic difficulties. It is easily differentiated from *aortic regurgitation* because of (1) the absence of marked left-sided hypertrophy, (2) the absence of the Corrigan pulse, and of the great pulse-pressure, (3) the absence of transmission to the vessels of the neck, and (4) the other incidental signs of aortic regurgitation.

It is true that the murmur of aortic regurgitation is frequently heard in the same location, but it is generally transmitted up to the right and down. In any case in which aortic regurgitation is present, it is almost always the predominant lesion, as far as physical signs are concerned. Nearly always when the diagnosis of pulmonary regurgitation is made on the basis solely of a diastolic regurgitant murmur, it will eventually turn out that the case is one of aortic regurgitation.

It is in connection with *mitral stenosis* that most difficulty may be encountered. In uncomplicated mitral stenosis the murmur is never heard so far up on the chest-wall. The slapping first sound, the reduplicated second sound, and the thrill—one or more of these sounds will always be present—serve to differentiate these cases. The Graham Steele murmur may be considered a functional pulmonary regurgitation. It is uncommon, confined to a small area and indistinguishable from organic pulmonary regurgitation.

Prognosis.—Here the prognosis depends upon the cause of the lesion. If it is due to relative insufficiency, consequent on other lesions, the outlook is not immediately serious. The prognosis must rather be based upon the condition of the right ventricle. If it reacts without pronounced decompensation, freedom from the immediate danger is assured.

Organic disease producing regurgitation is so commonly acute and so rarely chronic that little information is available upon which to base a prognosis. In general, however, it is to be predicated on the condition of the right ventricle, and consequently on the increase of tricuspid regurgitation.

Pathology and Pathological Physiology.—The mechanism of the production of this murmur is exactly similar to that of aortic regurgitation, except that the blood flows back into the right ventricle instead of into the left ventricle. Some hypertrophy of the right ventricle always follows. It is rarely an uncomplicated lesion, so that the postmortem changes are not distinctive.

By far the greater number of cases are due to functional dilatation and the microscopical changes are not very decided. The conus arteriosus and the right ventricle are dilated. There are other changes throughout the vascular system, but they are the same as those met with in broken compensation from any cause. Most of the cases are transient. One looks for the lesion most commonly in association with mitral stenosis.

GENERAL PROGNOSIS OF CHRONIC VALVULAR DISEASE

In view of the general consensus of opinion that in the late war soldiers who had valvular lesions and who had never developed signs of decompensation were just as efficient from a military standpoint as others, it seems unorthodox to maintain that such patients do not have as good a general outlook as to length of life as those with healthy valves. One constantly sees patients who have been rejected by insurance companies many years ago, and yet to-day are seemingly healthy and well; yet in the main it is these exceptions to the general rule which attract our attention. The cumulative clinical experience of the profession is to the effect that a large percentage, certainly more than a majority of patients with unmistakable organic valvular disease, sooner or later present signs of decompensation. When the valves are diseased, muscular disease, also, is always present to some degree. The heart may functionate properly for some years, until added infection puts a strain on it and decompensation occurs. The extra labor of the army and camp is not nearly as apt to bring this about as are the infections of civil life. The experience of the army has been that these patients were as strong as others, but that when a slight infection of any kind, particularly in the respiratory system, occurred, they commonly broke down.

Aside from its import in general practice, this matter of a proper evaluation of the significance of valvular disease becomes a vital one in life insurance examinations, and in industrial life. The necessity for a yearly examination of men who hold positions of such a nature that their sudden incapacitation would menace the life of others is quite apparent to all. Such men as engineers engaged on railway trains, boats or vehicles of any kind, boiler-men, motormen, conductors, switchmen, tower-men, elevator-men, telegraph and signal operators, chauffeurs, pilots, etc., are all in this category. It may be argued here that one might gauge their future health and reliability by the presence or absence of symptoms, at the time when they present themselves for a position, but such candidates are at pains to disregard or conceal any or all symptoms. For that reason the only practical solution is to rely upon such signs as are found on a rapid physical examination and to apply general principles of prognosis based upon these findings. As a general rule those who have a definite cardiac lesion should be prevented from engaging in any of these occupations even though individually the patient may be a good risk, because after all there is a slight appreciable risk in all of these cases. Insurance companies are often criticized for their attitude in this matter, but after all these companies are not organized for charitable purposes but rather to take only selective risks as far as human judgment can determine them, and no one can maintain that the subject of valvular disease is entirely normal.

The question which the patient usually asks on being told that he has a valvular lesion is, "Can I ever get well?" and in his mind he stores away at once the picture that there is a likelihood of sudden death for him. In answer to the first question one is justified in saying that practical recovery may be assured but that absolute recovery is a physical impossibility. The figure of speech that a face with a scar is quite as useful and quite as long-lived as one without a scar is a homely yet intelligent word picture which makes clear the relative harmlessness of the lesion; or again, the following picture sometimes makes it more clear to the patient's mind: "There are two trees of equal size and strength. A woodman makes a gash in one; it heals over, leaving a scar. Both trees are to all intents and purposes the same, as far as strength, seed-bearing properties, etc., are concerned, and continue so for years, but a severe storm is more apt to blow the injured one over than the sound one, because of the initial scar of many years previous. If the storm is a very severe one the perfect tree as well as the injured one is apt to be blown over." As a consequence of the lesion, with ordinary care the patient's life will not be shortened in the long run. At the examination his mind should be disabused of the idea that he has a weak heart. This is a term employed by some practitioners to explain the symptoms of muscular insufficiency, and by others as a means of conveying to the patient's mind the fact that he has an organic valvular disease, but in an endeavor to assuage his mind gives it this term. It generally serves to make the patient feel that the disease is not organic, and is only of a temporary nature. It is an elastic term which seldom conveys to the minds of any two patients the same picture, or the one intended by the physician.

The second question should be always discussed with the patient as soon as the diagnosis is made. He should be told that he has a valvular disease, but that he will not die suddenly. The prognosis, no matter what the lesion may be, can never be made with exactness. The best statement that can be made is that death is or is not imminent; in fact, the future prognosis can only be made with the addition of many "ifs." One may divide the prognosis as follows: (1) the ultimate prognosis, (2) the immediate prognosis, (3) the mode of death. Of course, this should not be fully discussed with the patient. The *ultimate prognosis* is of importance, for ahead looms the possibility of change of occupation, and the question of marriage and pregnancy. In the young the questions of exercise, and sports, climate, etc., must be considered.

The *immediate prognosis* has to deal with the problems presented when there has been more or less evidence of failing compensation. Very many more factors enter into this problem than into the first mentioned.

The third question is that of the *mode of death,* and the possibility of sudden death. While the mode of death can often be foretold, the question of the likelihood of sudden death is always perplexing, inasmuch as the changes which immediately precede this event are microscopic rather than macroscopic.

In general, one may base the ultimate prognosis of heart disease upon five general conditions:

(1) The ultimate cause of the heart lesion.
(2) The condition of the arteries and kidney.
(3) The portion of the heart involved.
(4) The person who has the disease.
(5) The treatment he receives.

From a prognostic standpoint it may be stated that symptoms are of far more importance than physical signs.

Cause of Cardiac Lesion.—The ultimate causes of cardiac lesions as seen in active hospital service may be roughly grouped as follows:

Rheumatic	70 per cent.
Syphilitic	15 "
Arteriorenal	15 "
Secondary to diseases in other organs (lungs, thyroid, etc.)	5 "
Congenital	negligible

Cabot estimates thus:

Rheumatic	45 per cent.
Syphilitic	12 "
Nephritic	20 "
Arteriosclerotic	15 "
Goiter	5 "

Recurring "Rheumatic Carditis."—Acute cases in children with fever, particularly those with pericardial involvement, are always serious. Those *without* temperature elevation over 100° F. (37.77° C.) are not in any immediate danger. It is only in the case of those presenting considerable temperature elevation and severe general symptoms that we need worry as to the immediate future.

Rheumatic Fever.—Rheumatic involvement of the heart offers a favorable prognosis as compared with other forms of heart disease. This is particularly true when the valves are the portions of the organ which are the most affected; in such cases the patient is forewarned to keep quiet, and no such warning is given in silent cases. The effects on the myocardium are more transient than in other infections, but are more apt to be repeated. Therefore, the older the patient is at the first break in compensation the better is the outlook, for reïnfection is correspondingly less likely. As a rule such hearts have from 15 to 20 breaks in compensation before the fatal termination occurs. They may go on for years functioning quite well after one or more break-downs which because of the presence of extreme edema, hemorrhage, etc., are so severe that life is despaired of.

The presence of infection of any kind is usually the determining factor in the break-downs. Consequently the less frequent any such infection is, the less likelihood there is of a fatal termination, and, on the other hand, the more subject the patient is to such infections the more rapidly the end comes. The course of the lesion is a series of repeated acute attacks rather than a steadily progressive process.

SYPHILITIC CASES.—As a rule the early syphilitic manifestations are not serious. The heart or vessels are involved in 50 per cent. of all cases of syphilis. Its effects are positive and generally progressive, unless treated.

In heart disease due to *untreated* syphilis one may tell the patient that the lesion occurred about fifteen years before the onset of the symptoms, and warn his friends that he has at most three years longer to live. Treatment is only palliative.

In *treated* cases, of course, this general rule does not apply, about five years being the ordinary period of life expectancy after the onset of symptoms. Once symptoms are manifest, they may be ameliorated, but it is impossible to dissipate the permanent organic changes. With the exceptions of gumma, treatment is only partially successful. The symptoms may be modified, especially if the pain is due to lues, and life will be prolonged, but tissues cannot be made over again, as is the case in some other parts of the body, in which syphilis reacts marvelously to treatment. Frequently improvement is only noticeable after some months of treatment. If marked broken compensation has already occurred, the patient seldom lives more than one year, and usually much less. The number of recoveries from attacks of decompensation is rarely more than three, differing from rheumatic carditis, from which there are so many recoveries after breaks in compensation.

ARTERIOSCLEROTIC FORM.—Cases associated with high blood-pressure are so closely related to kidney disease on the one hand or to syphilis on the other, that it is difficult to lay down dogmatic rules as to progression. If the high blood-pressure is a family trait the course of the disease is likely to follow whatsoever course the family mode of death has usually been due to, *i.e.*, one of the material accidents, as (1) cerebral hemorrhage, (2) nephritic death, or (3) cardiac death, each running its own course. In general the outlook is fair if the lesion is due to something which can be corrected by hygiene or medicine. If it is due to renal disease there will be a steady progressive advance. The height of the pressure is not of so much import as its course. If it steadily rises in spite of everything the outlook is unfavorable. A marked fall in pressure without cardiac improvement is serious. Stout patients with high blood-pressure, dyspnea, and traces of albumin look like hopeless cases, but if they can take care of themselves they often live for years. Any infection, however, is likely to carry them off. The author believes that in the past we have viewed these cases too seriously. The more experience one has the more hopeful one becomes as to the outcome. Cases which are progressive during the first few months after the onset of the symptoms are apt to progress badly, but these are comparatively rare. In cases which are slowly progressive, with intervals of well-being, if properly treated, live for many years, and, in some instances, they may even go back to strenuous occupations provided a long rest is enjoined. In general, the better the financial status of one's clientèle the better the prognosis in this group, because the patients are better able to take care of themselves and do not have to worry about the necessities of life. The hospital patient who suffers from high blood-pressure and valvular disease does not long survive his first attack of decompensation.

Kind of Person Who Has Heart Disease.—The man who can take things easy and who readily learns a lesson always has an advantage over his nervous and fretful brother. Heredity and environment are two great factors which must always be considered in making the prognosis.

Heredity.—Aside from acute infectious attacks, heredity counts for more than anything else. The patient whose family history is free from cardiac disease has a much better prognosis than the one whose progenitors have had the disease. A family tree with one or more roots involved by cardiac disease means that the infection has been passed on, or at least that the susceptibility to the rheumatic poison is established in the offspring. Such patients are more apt to have severe attacks. The *anemia* which is present in all victims of cardiac disease is an index of the patient's reacting power to the virus, and, of course, his heart-muscle is correspondingly affected. In the case of those who suffer from severe anemia the disease is apt to be serious and the heart-muscle is correspondingly deprived of rich blood, in other words, pale cardiac patients are apt to die. If anemia occurs for the first time in the course of an acute exacerbation, grows steadily worse and does not react to treatment, it is sure that the patient will not long survive. This is especially true in aortic regurgitation. On the other hand, if it appears late, and reacts to treatment, it has no evil prognostic import.

Environment.—The presence or absence of repeated infection, susceptibility to cold in the head, chest or tonsils, are all grave handicaps. A head cold or a tonsillitis often causes an attack of fever in these patients, and frequently precipitates a fatal issue. The presence of chronic foci of infection, such as teeth, tonsils, sinuses, prostate, uterus, etc., is a factor to be weighed seriously. Nor must the condition of the stomach and digestive tract be disregarded in arriving at a conclusion. Ability to sleep is always a good omen, no matter how threatening the case may otherwise be.

OCCUPATION.—Occupation is of prime importance, although the author believes that it is of less importance than frequent mild infection. Certainly the continuance at any occupation or work which induces any of the symptoms of disturbed compensation must be weighed seriously.

CLIMATE.—In general the prognosis is worse in the winter and in the cold weather than in the summer. The same rule applies as to climate in general. Damp, cold climates are much less favorable than dry, warm climates.

AGE.—In young children the outlook is unfavorable; not only do many such patients die of acute carditis, but they are apt to have repeated attacks which damage the valves irreparably. Endocarditis in a child under six years of age, if associated with symptoms, usually foreshadows a ruined life. Combined valve lesions are also very serious, because malignant endocarditis is more likely. In elderly patients the outlook is better, because the older people take better care of themselves. Old hearts are more easily trained than young ones. Worry and excitement have a very bad effect, and lead to breaks in compensation, especially in aortic disease. In such cases the usual sequence of events is:

(1) Symptoms of coronary lesion.
(2) Nephritis.
(3) Myocardial weakening.

The three parts of the circulatory tree, heart, arteries and kidneys, are so closely related that injury to one is practically always the concern of all. The condition of the arterial system is of as much import as the condition of the valves of the heart. As long as the arterial system is in good condition there is little cause for alarm. This is usually the case in compensated mitral disease, and is one of the chief reasons for its comparative harmlessness. When young patients show signs of arterial involvement the outlook is indeed gloomy. In those over fifty years of age the presence of sclerosis is not of so much import. The older the patient the better the outlook. Death from cardiac disease is more common among those of middle age than among the aged.

The kidney forms the third root of the trilogy, and while it is of relatively less importance than the heart or arteries during the early periods of life, in the case of those advanced in years it is of quite as much import. When decompensation occurs in a patient with a contracted kidney the result is more hopeless than is the case when any other single complication is present. If the kidney is large and white, almost any severe inflammatory disease nearly always leads to an immediate fatal termination. This is especially true when the valve lesion is that of aortic regurgitation. Generally speaking, primary kidney disease which presents dyspnea on exertion as an early symptom produces death from cardiac insufficiency.

The earliest sign of broken compensation is the presence of fine râles at the base of the lungs when the patient sits up after having been in a recumbent position for some hours.

Another way of determining the onset of broken compensation is by the disappearance of the pulse when the arm is elevated above the head. Abrahams has called attention to the fact that in mitral disease, usually before there is a break in compensation, the pulse can be felt as well in the elevated arm as in the lowered arm. At the first sign of failure, there is a marked difference in the quality of the pulse in the elevated arm. When there is a decided break in compensation the pulse in the elevated arm disappears entirely. Of course, the weakening of the second pulmonic sound is a positive evidence of impending failure, and is, when it can be determined, of more consequence than any other of the signs mentioned. In this case, symptoms are of more importance than physical signs. Dyspnea is the most valuable single symptom as a basis for prognosis. Cheyne-Stokes breathing, although not serious in itself, is of evil import, and the patient seldom survives for long, if it becomes noticeable during waking hours. If it disappears and is followed by rapid breathing, death is not far distant.

Conditions Affecting the Prognosis.—MURMUR.—*General Considerations.*—The relative softness or loudness of a murmur has no significance, although, in general, the murmur which was soft and becomes harsher is a good omen, as it indicates an increased muscular force. And, per contra, the loud murmur which does not entirely displace the first sound of the heart in mitral regurgitation is a good sign. One which does not entirely displace the second sound of the heart in aortic regurgitation is also a good sign. A loud and well-transmitted murmur, even though it entirely displaces the second sound of the heart at the apex or at the base, has a fairly good prognosis. Occasionally, in children who are rapidly growing, this does not hold true. A weak murmur which reacts to digitalis and remains loud, indicates that there is no immediate danger. When such a murmur becomes strong on digitalis stimulation, but quickly returns to its former state, the outlook is not encouraging.

The average length of time from the formation of a lesion to break in compensation has been variously stated as from seven to fifteen years.

COMBINED LESION.—When these are on the same side of the heart, they are worse than when on opposite sides.

The most dangerous combinations in order of frequency are:

1. Aortic regurgitation and mitral stenosis.
2. Aortic stenosis and mitral stenosis.
3. Aortic and mitral regurgitation.
4. Mitral regurgitation and mitral stenosis.

In passing it is well to point out that it is unsafe to diagnosticate involvement of more than two valves in any patient.

The last three are fairly common, and are, of course, very much more serious than single lesions, as it stands to reason that the myocarditis is much more extensive.

Patients suffering from grave heart disease will sometimes pass through a serious infectious disease, but during convalescence they are apt to go to pieces. This is especially true in *pneumonia.* They frequently pass the crisis satisfactorily. Patients with valvular disease, but who have not had any evidences of broken compensation, usually recover from ordinary lobar pneumonia in approximately the same proportion of cases as among normal individuals. In those, however, who have previously shown decided symptoms of decompensation, recovery is uncommon.

Bronchitis in a patient with valvular disease always requires serious watching. It is almost as grave an infection in a patient who has shown signs of decompensation, as an ordinary pneumonia in a previously healthy individual.

When *bronchopneumonia* occurs it is usually a terminal event. When true epidemic influenza attacks a cardiac patient who has suffered from broken compensation, it is accompanied by a very slow convalescence, which must be measured by months rather than weeks, and the patients rarely ever completely recover. If bronchopneumonia occurs, death is the rule.

In *erysipelas,* when there is no disturbance in compensation, the outlook is favorable. When decompensation is present it is a very serious complication. Acute *pericarditis,* even with extensive effusion complicating an old valvular lesion, generally presents a good prognosis, although it is apparently a very desperate combination.

In general the outlook is favorable in *pregnancy.* If compensation has been broken it is a serious problem. When mitral stenosis is present the outlook is much worse than in the presence of any other valvular lesion. Especially is this true with regard to the infant. Death may occur suddenly toward the end of pregnancy, and usually comes on as the result of pulmonary edema. Early in pregnancy physiologic abortion is the rule. Labor itself does not add greatly to the strain of the heart, and is not in itself of serious import.

Jaundice, if hemolytic, is a bad sign.

Acute *inflammation of the gall-bladder,* just as any other infection, is often the cause of a fresh attack of endocarditis and death.

Psychoses, when they occur with aortic disease, are not immediately serious. When they are marked in mitral disease they usually indicate that death will occur within a few weeks.

Dropsies, if not of long standing, commonly result, at least during the early attacks of decompensation, in recovery, and the patient may live for years, but when there is fluid in the serous cavities, it does not rapidly disappear. The patient does not usually survive for many months. As far as immediate improvement is concerned the public hospital patient has in general a better outlook than the private patient, because he has not been under treatment and has been living an unhygienic life, and may therefore react satisfactorily to more favorable conditions. The reverse is true of the private patient, who has, in many instances, already used all of the therapeutic resources and has had most of the advantages of proper life and surroundings, without avail.

The patient who does not promptly react to rest in bed, opiates, and two or three days of intensive digitalis therapy, generally offers a grave prognosis. If improvement occurs after rest in bed alone, the outlook is not as favorable as it is if it follows the use of digitalis. It is difficult to account for this on a physiological basis, but this is a clinical observation. In general the pulse-pressure increases, and the frequency is reduced in all except the aortic cases as the patient improves, and *vice versa.* A decompensated heart-beat which does not fall below 90 after prolonged, careful treatment during two months will probably never result in recovery.

When heart-failure cells are found in the sputa the disease is far advanced. Spitting of blood is not serious if the compensation is good, but when it is very profuse and continues for several days, recovery is the exception. The same is true to a lesser degree in the case of nose-bleed.

Infarcts are always dangerous; if septic, they are fatal. About one-third of all patients with cardiac involvement have at some time or other suffered from such infarction.

Unless fluid is present, *pleurisy* is not of much significance.

In early broken compensation the immediate prognosis depends upon:

(1) The extent of stasis in the lungs. This can be measured by:
  (*a*) The amount of dyspnea and the inability to take a long breath.
  (*b*) Cyanosis.
  (*c*) Râles at the base of the left lung after the patient has been lying on his back for some hours.
  (*d*) The condition of other organs: the size of the liver, and the quantity of urine.
(2) The condition of the auricles:
  (*a*) Size, dilatation, measured by the extent of dulness in the cardiohepatic angle and at the base of the heart.
  (*b*) Functional activity—*fibrillation.* This generally indicates that the patient has on the average about five years to live, seldom more than ten. The older the patient when the fibrillation occurs the better the outlook.
(3) The condition of the ventricles, especially as to the presence of high arterial tensions, bronchitis, and other complications.

Commonly death is a slow process in heart disease. It is usually associated with pulmonary edema, and in almost every instance there is some terminal infection, generally a pneumonia or nephritis, less frequently an acute endocarditis or enteritis. Usually death is brought about through an added disease of some other organ. If the condition is acute it is to be assumed that the lungs are responsible; if it is chronic, that the kidney is to blame. Sudden death without any warning may occur in any form of heart disease, but it is comparatively rare. Nearly always there are warning signs within a few days before the fatal issue, although the warnings may be so slight that they are commonly overlooked. Aortic regurgitation furnishes the largest quota of sudden deaths without any marked warning, but even here there may be danger signals in the shape of attacks of stenocardia. About 40 per cent. of cardiac syphilitics die suddenly, and this is one of the frequent causes of sudden death without much warning. In about 2 per cent. of the cases of mitral stenosis the patients die suddenly. In the latter case, death usually occurs in a patient who is in bed during the attack of broken compensation and who is apparently doing well. On sitting up suddenly he falls over dead. In mitral cases an *x*-ray picture of the heart lying flat on the diaphragm is the only physical sign which gives warning of such a possible ending. A sign of some value in a patient who has not been under digitalis is as follows: One hears the two sounds of the heart. After the second sound one wonders if the heart will ever beat again, the interval being so long and the rhythm seeming to have stopped. This same phenomenon is also present in a heart thoroughly digitalized. Many of the patients suffering from mitral stenosis die of embolism, especially cerebral embolism. In such cases death is not sudden. In pulmonary embolism death is also delayed, usually for from fifteen to twenty minutes after the onset of the embolism.

Angina pectoris is the disease commonly associated with sudden death and yet, as compared with the frequency of the affection, it is not so immediately fatal as was formerly taught. It is, however, always a step toward sudden death. In any case of heart disease, with severe pain about the heart, even though it has none of the characteristic radiations of angina pectoris, if the pain is not speedily relieved by large doses of morphin a fatal issue within a few hours is at least a strong possibility. Repeated attacks of cardiac asthma, which is another term for acute suffocative pulmonary edema, in conjunction with symptoms of vomiting, diarrhea, delirium, and marked mental wandering, often foretell the near approach of death, but it is relatively seldom that these patients die during the attack of acute pulmonary edema itself.

Large, stout patients with small hearts lying flat on the diaphragm, accompanied by a weak and rapid pulse, a systolic murmur at the base, and a general arteriosclerosis, are most liable to die suddenly. The minor symptoms of which these patients complain are not apparently any worse just preceding death than they have been for weeks and months previous, but on close questioning it will be found that some unusual strain has been placed on the heart just preceding the fatal issue; this is commonly a large, indigestible meal or some physical exertion, such as running up stairs, or some anxiety.

GENERAL TREATMENT OF VALVULAR DISEASE

Cases Discovered by Accident and Presenting No Symptoms

When in the course of a physical examination one meets with a patient who has a valvular lesion, with or without a history of a break in compensation, and who yet presents absolutely no symptoms when examined, what course should be pursued?

Of course no one will advise medicine for a patient who presents nothing but a murmur of which he may or may not be conscious. From a practical standpoint, however, the patient should be informed of the presence of the murmur, with a proper explanation of what it signifies (see General Prognosis). This opens up a large question. That patients occasionally suffer much worry and annoyance from such a knowledge is undoubtedly true. On the other hand, no one can deny that it may be of more lasting value to the patient, as far as life itself is concerned, if he knows that a cardiac lesion is present. The worry may annoy him, but it will not materially shorten his life. It is customary to say that there is no danger to a man who has a compensating valvular lesion, but experience teaches us that sooner or later, due to either a fresh disease of the valves or to strenuous exercise, most of these patients will (if they live long enough) become victims of broken compensation. Thus, a patient with a valve lesion is a potential cardiac invalid, no matter how well he may be at the present time.

Cardiacs should avoid heavy occupations; the constant use of the arms; dusty trades, or working places where infections are common, also public places, as churches, theatres, etc., and occupations causing much nervous strain. Any exercise not producing breathlessness, pain nor general distress, is to be recommended. If possible, he should seek a warm climate in winter. In those subject to repeated colds, it is worth while to try the injection of stock influenza vaccines twice a year.

He should be taught the seriousness to him of slight infections, inasmuch as they are always more likely to light up disease in his valves than in those of a normal individual. He should also be warned not to undergo severe physical strain. On the other hand, there is no indication to lessen the ordinary duties of his avocation. If the patient is a child and does not present shortness of breath or palpitation on strenuous exertion, no special restriction as to ordinary games is necessary. He should be prevented, however, from taking part in the strenuous forms of exercise, such as football, rowing, running, etc. His occupation should be selected so that hard labor will be avoided. In all patients in whom such a lesion is discovered, general directions should be given to prevent a recurrence of the disease which is primarily responsible for the valvular lesion. If syphilis is the cause, the systematic bi-yearly use of **antiluetics,** and the **avoidance of alcohol** (see Treatment of Broken Compensation) are important. If arteriosclerosis is the cause, the employment of **a suitable dietetic and hygienic regimen,** and the intermittent use of **potassium iodid** should be instituted.

He must be taught that for him **sleep** is more essential than food; that he should have at least nine hours rest in bed every twenty-four hours; that such rest is the only savings bank account against the likelihood of decompensation. Unfortunately, a tendency to insomnia is usually present, and sleep must often be wooed (1) by the familiar drink of hot **milk** at bed time; (2) by **alcohol,** either in the form of beer or whisky; (3) by a hot **bath;** (4) by **bromides.** Inasmuch as we are now discussing the potential invalid, rather than the actual one, one does not resort to the stronger soporifics.

Unfortunately most cardiacs have an unrestrainable desire for motoring. This should be vetoed in every case where there has been a break in compensation. This is so because of the likelihood of nervous shocks, as well as the physical jolting of motor-car driving and riding. If such a patient insists on motor-car journeys, then he should have his back to the driver, so as not to see the many near-accidents that daily occur.

Inasmuch as fully two-thirds of the cases of valvular disease met with in practice have their origin in previous attacks of rheumatic endocarditis, it will be admitted that the **prevention of rheumatic endocarditis** is the most logical step. Unfortunately the contagiousness of acute rheumatic fever and of the endocarditis which follows it is not sufficiently appreciated by the profession. The author has scarcely ever met with a frank case of rheumatic fever or rheumatic endocarditis in a child which could not be traced to a previous infection in the rheumatic parents, grandmother, nurse, or some one who had charge of the child. In adults it is more difficult to trace the infection.

The history of exposure is almost, if not quite, as important as it is in tuberculosis, so that the first step in prevention is to prohibit anyone who is suffering, or who has suffered from rheumatic fever, from coming in constant and close contact with small children. In practice an old grandmother is the common carrier of infection.

Once the patient has been infected with the virus of rheumatic fever, the condition in that individual is somewhat analogous to one infected with lues, in so far as that symptoms are apt to reappear whenever there is a lowering of the resistance from any cause—whether it is infection, worry or overwork—so that "once rheumatic, always rheumatic."

In the present day the pathology of chronic cardiac disease, particularly of a valvular and muscular type, does not carry with it the same conception that was formerly had. Formerly it was believed that chronic endocarditis, as well as other chronic diseases, was a progressive disease, that is, that the pathological lesion was constantly extending. After all, chronic processes become worse mostly by acute exacerbations, due to many kinds of infection—that is, after the primary attack each succeeding infection, not necessarily the same as the first, pushes the patient on a little bit farther, but in the interval no appreciable progress downward is made. In the development of an acute decompensation, in the past it was believed that some strain, usually of a physical character, was necessary. At the present time the opinion is that overstrain is, with the exception of an occasional decompensation in the primary form of mitral stenosis, a comparatively rare cause of heart failure.

Pain and dyspnea act as checks to overstrain in most instances, and if overstrain does seem to induce heart failure it may be explained that the strain has opened up an avenue of infection, thus precipitating heart failure; because with heart failure of a progressive type temperature almost always occurs, and it would be difficult to picture strain *per se* as a cause of temperature. A more satisfactory explanation is that an acute infection was already present somewhere in the body at the time, and the strain merely explodes the infection. In fact so rarely does exertion of itself without infection produce cardiac failure that with the exception of decompensation of primary mitral stenosis it may be dismissed as almost non-existent.

As to the form of infection, in more than seventy-five per cent. of the cases the cause is an acute infection of the air-passages. It is to be understood that the infection is usually an acute one; because of the frequency of chronic foci of infection as a cause of disease it is easy to be confused. If rectal temperatures be taken during the attacks of decompensation, there will always be found an average increase of from one-half to one degree above normal. Close inspection of the throat, mouth and nose will reveal either a simple inflammation or, more commonly, one with some of the characteristic influenza signs, viz.: (1) Redness of the outer palpebral area of the conjunctivæ; (2) redness of the anterior pillars of the fauces, varying from pink to carmine in color; (3) injection of uvula; (4) papules on the uvula and post-pharynx; (5) Steno duct enlargement and injection of the same as though a pin had been inserted into it; (6) other hemorrhagic areas in the mouth; (7) cyanosis of the lip edges, and oftentimes of the skin under the nails. In some instances only a few of these signs are present. It is rare to find them all present except in severe influenza.

Both sides of the nose should be inspected, and even the ear drums. It is not sufficient to inspect the nose alone, but if in doubt a swab should be passed up behind the uvula, and the presence of blood on it will often disclose the fact that there is an open area in the naso-pharynx that escapes the naked eye.

It is estimated that from sixty to seventy per cent. of office patients in the winter show these head signs, and yet most of them are unconscious of having a cold in the head.

It is a well-known observation that cardiacs seldom die in the summer-time from cardiac accidents. One may say that infections are at a minimum in the summer. The United States Public Health Service has shown that such influenzal infections are most frequent in almost all parts of the United States in October, followed by a decline until the latter part of December, at which time another outbreak occurs. Usually there is some increase in March and in the latter part of May. Annually ninety per cent. of the population averages between three and four head colds a year.

We always charge up the sudden death occurring in the winter-time to the cold weather, when a cardiac patient gets up feeling well in the morning, goes out into the cold, and drops dead at the top of the subway stairs. Not a few of these, if examined in a routine manner, present unmistakable evidence of carrying infection in their fauces. It is not claimed that all of these patients in whose mouths and throats one sees in the course of a routine examination the evidences of an acute respiratory infection, will develop the palpable evidences of a head or chest cold, but in following up these patients one always finds (1) that someone else in the family has had or will have a troublesome head cold, or (2) that within a few days the patient himself will experience one. A few will merely act as carriers, and if the exploding agent, whatever it may be, whether exercise, mental disturbance, or what not, does not occur the patient is none the wiser as to his being a carrier. Piles, acne, conjunctivitis, or any raw surfaces should all be examined closely. If any such surfaces be found they should be treated and healed, as until they are healed and well the endocardial attack will not progress favorably.

The problem will often arise as to when does the fresh endocardial lesion begin in the course of an infection. In an influenzal infection it is often not so difficult to decide, because the regular three and one-half day rise of influenza comes with great regularity. The presence of a steadily continuous type of temperature, or with daily excursions, would point to the existence of an acute endocarditis.

This cold, or influenza, will seldom be stressed by the patient, and one must instinctively look for the evidence in the throat, nose and eyes.

Granting that such an infection is found, the first principle is to stimulate nature to repair the damage done.

Some one will raise the time-old issue that painting or even spraying the mucous membrane of the throat and fauces has little or no effect on the disease process itself, and that its effects pass off quickly. Inasmuch as these red areas are the only evidences of a focus of the disease, and the disappearance of all of these inflamed areas, so far as we know, occurs simultaneously with disappearance of all of the signs of the disease, a connection seems assured. The blanching following silver application and the red reaction thereafter is proof positive that the effect is not transitory. The fact that there is almost always present a coincident slight inflammation of the conjunctiva would speak for the constitutional character of the infection—i.e., that these mouth signs were merely the local expression of a constitutional disease, and that only by vaccines could sufficient immunity be readily established, just as we hope to establish local immunity by the use of counter-irritants, such as silver and iodine salts. Unfortunately at the present time there is no unanimity as to the particular organism that causes any of these infections, and one would be acting blindly in resorting to vaccines. However, there can be no valid objection to trying a stock vaccine if one is striving to produce a protein shock reaction. In doing this, great care must be exercised, because surely no one would care to produce a shock reaction in a decompensating cardiac. Some cases react well to vaccines, but we do not as yet feel like recommending the procedure as a routine. About five minims of an influenzal combined vaccine given subcutaneously is ordinarily safe, and free from disagreeable by-effects.

At present one's chief hope is in establishing local immunity, and thus causing disappearance of the local lesions, as noted in the mouth, by means of irritants.

Where for any reasons an irritant cannot be employed, then the use of organic silver compounds is justifiable. Such organic salts have some value as a cleansing agent, but the real inflammation in these cases is beneath the superficial layer of the mucous membrane, and therefore is not reached by the treatment. Any irritant, no matter what it may be, is of much service. It accomplishes results because of a local chemotactic effect on the leucocytes. The handiest remedy is silver nitrate, say in two, or even ten per cent. solution. Of all irritants it more nearly possesses the qualifications sought for, because of its penetrating at least beneath the superficial layer of mucous membrane and coagulating there. The preparation should be painted carefully over all of the red spots, no matter where they may be, mouth, throat, nose, pharynx, etc. The discomfort disappears within a half-hour, and the patient should be warned of this discomfort. If the patient is too sensitive, a preliminary painting with cocaine may be done, but this does not seem to produce the same results as when the membrane is not prepared by the cocaine. Instead of the silver solution an iodine preparation, preferably inorganic, and not strong enough to produce excoriation, will accomplish the same results, or if the practitioner likes an iron salt, it will answer quite well. Where painting is not feasible a spray of the same solution, but of weaker strength, is advisable. Such irritants should not be applied too often, or else nature will be stimulated beyond her reactionary powers. Once or twice a day is all that is necessary. The inhalation of chlorine gas for the same purpose has not activated the result that was hoped for.

The next most likely place of an acute infection, in the absence of any kind of respiratory infection, is the kidney. A close examination of the urine will in not a few of these cardiac breakdowns reveal a moderate amount of pus, and often a few red blood cells. Here again the question will be raised how one is to tell pus from white blood cells. A good working rule is that if there are more than fifteen cells to the field it is fair to assume that an inflammation of some kind along the genito-urinary tract is present. This is so often true as to be the rule rather than the exception.

In the cases that are due to kidney inflammation frequently hexamethylenamine is a useful agent; in others alkalinization of the urine. In the bowel cases the use of frequent doses of castor oil, calomel, irrigations, and of suitable dietary will be of service.

As to the digestive tract, it is true that most cardiacs in the stage of decompensation from any cause manifest digestive syndromes. These occur as a result of the disease and not as a cause, but the presence of either abdominal pain or diarrhea is strong evidence that gastro-intestinal infections are a likely cause, and may precipitate heart failure. In the rare cases that do not have either respiratory or kidney dysfunction, and in the absence of any other manifest signs of acute infection, our attention should be centered on the gastro-intestinal tract.

So that, to sum up, in any case of decompensation in cardiac or of vascular disease, whether it be endocarditis or endarteritis, one should endeavor to fathom the cause of the immediate breakdown: (1) the mouth and throat, and even nasopharynx, should be closely inspected, even with a swab if necessary; (2) the urine should be examined for blood and pus cells; (3) the digestive tract from mouth to anus should be queried; any eruption such as pimples, piles, etc., should be carefully considered.

By the addition of this schema of therapy one more line of treatment is added in an attempt to lessen the long illnesses so common in the life history of the cardiac.

This is a much more rational way of treating an immediate cardiac breakdown than by trying to treat the heart itself, by digitalization alone, as is usually done. By this the author does not mean to criticize the use of digitalis, but in most instances its value is only secondary. It is much more rational to heal the point of origin of the acute infection than to treat the results.

FOCAL INFECTION.—Of course these common infections are more apt to occur in patients suffering from diseased tonsils, adenoids and deflected septa. Rarely some other focus, as gall bladder, pus tube, sinuses, etc., is present. As to focal infection itself, there is no positive evidence that removal of tonsils, adenoids, teeth, or any other focus, prevents recurrence of acute rheumatic endocarditis as such, except in so far as it lessens the likelihood of infection from those sources.

That the removal of infected teeth and such foci is followed by freedom from attacks of endocarditis or rheumatic fever is quite true, but inasmuch as such infections fail to recur under other conditions there is no scientific proof as to their cause and effect. However, the removal of enlarged tonsils, adenoids and deflected septa does have a positively good effect, and it is largely because it lessens the chance of acquiring fresh infections, and the frequency of breaks in compensation depends in direct proportion upon the number of such infections; in other words, no infections, no fresh endocarditis, no loss of compensation. This is a working rule which is not absolute, but is practical, as all who have had endocarditis are likely subjects for fresh attacks and consequent breaks in compensation. Such patients should be under frequent observation at stated periods throughout the year. In this way only can the minor symptoms be noted, and advice given so as to prevent major breaks in compensation. The same advice holds good to a greater degree for those who have had an attack of lost compensation.

This becomes an economic subject of great importance from the hospital standpoint. A patient who has had a break in compensation and recovers sometimes goes back to the same environment and work after his discharge. Sooner or later he has a relapse, so that he is seldom out of the hospital for more than three or four months at a time. This is an economic loss both to the wage-earner and to the public. To prevent this, such a patient, upon his discharge, should be instructed to return to his physician at least once every two months for instruction and advice, no matter how well he may be. If the above picture is presented to him, his coöperation may be secured.

In this way the number of hospital days in the life of a cardiac patient is less than one-fourth of that which would otherwise obtain. Incidentally he is able to support himself and his family that much longer, and prevents them from becoming a charge on the community.

Cardiac clinics are of even more practical value than the tuberculosis clinics now so generally utilized, because prevention of loss in compensation in cardiac patients is a far more practical achievement.

Outline of Treatment of a Case of Valvular Disease (When Discovered by Accident With or Without the History of Previous Loss of Compensation) No Symptoms Present:

(1) Occupation—work to depend upon the reaction to exercise.
(2) Long period of convalescence, when recovering from recent attacks.
(3) Selection of climate and delimitation of exercise.
(4) Clothing of wool, to prevent return of rheumatic fever, avoidance of dampness, bed treatment for even the mildest infections.
(5) Food—plain and such as is not likely to produce flatulence.
(6) Regular bowel action—aloes or cascara as required.
(7) Treatment of any form of rheumatism by salicylates.
(8) Tonics as required—iron, arsenic and cod-liver oil.
(9) No restriction on tobacco or coffee if used in moderation.

Cases Presenting Minor Symptoms Which Accompany Valvular Disease

In practice the murmur is most commonly discovered in patients who present themselves for the treatment of what appears to be a minor complaint in some other part of the body, perhaps far removed from the heart —a symptom which at first sight may have little direct connection with the heart. The evaluating of the relation existing between such symptoms and the heart as a cause constitutes the highest art in medicine. For instance, one must not jump to the hasty conclusion that, because a murmur is present in the heart, the presence of the gastric symptoms complained of by the patient is necessarily a consequence of this lesion; but on the doctrine of chances it is very likely, unless there is direct proof that there is no such connection. In most cases the major cardiac symptom can be handled by the tyro perhaps as well as by the most experienced practitioner. It is in the management of the minor symptoms that experience is of value. Here the difference in success lies not so much in the difference of remedies employed as it does in their proper dosage and attention to detail, particularly in the matters of diet and hygiene, and in the prompt recognition and relief of these minor complaints. In the type of cases now under consideration the onset has usually come on following a head cold. Treatment even here should begin with absolute rest in bed for a period of several days. This entails the taking of meals in bed and the use of a bedpan if possible. The patient seldom feels that his complaint is sufficiently severe to warrant such a measure, but infinitely better results are obtained in the treatment of any of the symptoms by this measure than by half-hearted proceedings, such as partial rest and the internal administration of medicine. They will often follow such advice of the doctor if he is firm and positive in the matter. Absolute rest in bed for at least three days constitutes the best initial prescription for all such minor symptoms. Medicines may be used as an adjuvant, and will be considered later under the Treatment of Special Symptoms. This physical rest must be supplemented by mental rest. Visitors should be barred, and only absolutely necessary reading should be permitted.

Special Indications.—The value of the salicylates in arresting the consequences of rheumatic disease in the heart has not been proven. Unless there are undoubted evidences of rheumatic fever, they are not indicated, as they commonly upset the digestive tract. That large doses of salicylates given early and often prevent endocarditis is a fallacy.

The cases associated with arteriosclerosis and discovered before the onset of major symptoms offer a wide and fruitful field for the introduction of hygienic and dietetic therapy. (See Treatment of Arteriosclerosis.) Here small doses of **mercury** and **iodid** should be administered from time to time. Experience has shown that even where there is not the slightest reason to believe that lues is present, beneficial results frequently follow their use, even though we cannot give a satisfactory pharmacological explanation. It is at this stage of the disease that the victims of valvular disease due to syphilis are usually brought to our attention. When there is a well-marked history of previous infection, whether or not there has been a positive Wassermann, the patient should be subjected to **vigorous antisyphilitic** treatment.

Very often the relation between syphilis and the present valve lesion is not so clear. The Wassermann reaction, when present, is of course conclusive of former syphilis, but a very large percentage of undoubted syphilitic cardiac lesions are associated with a negative Wassermann, so that only positive tests should be counted. It is, of course, possible for a patient to have syphilis and an added infection of rheumatid fever or arteriosclerosis from other causes. In such cases one follows the teachings of clinical experience. The presence of uncomplicated aortic insufficiency, unless there is positive evidence to the contrary, warrants the use of antiluetic treatment. The same holds true to a lesser degree as in the case of aortic stenosis. While the combined mitral and aortic lesions are commonly rheumatic, yet even here as well as in uncomplicated mitral disease late investigations show a high incidence of syphilis. In all cases in which there are luetic lesions in other parts of the body, particularly in the shape of small white luetic scars in the mouth running down to the edges of the lips (and these should always be looked for), areas of leukoplakia, or hardness of the testicles, luetic treatment should be administered. In any case in which there is a history of syphilis, even though the lesion is unquestionably non-luetic, the patient should have the benefit of antiluetic treatment. On the doctrine that once

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.
PRACTICE OF MEDICINE—TICE

syphilis occurs there are always traces of it, every patient who has once been affected and who now suffers from valvular disease should have the benefit of treatment. In hospital practice syphilis should always be considered as a likely cause, whereas in private practice it is comparatively rare; it is more often missed from a diagnostic standpoint among so-called respectable people than in hospital practice. In those cases in which only pain and slight dyspnea on exertion have been evident, the use of **salvarsan** has been found most satisfactory. The dosage should begin with 3 decigrams (4.63 grains); after this six decigrams (9.26 grains) may be administered. One begins with this small dosage because occasionally cardiac patients do not bear the drug well. When serious accidents occur, a coincident involvement of the arteries and kidneys is usually responsible; hence, before the administration of the drug a careful urinary examination is an absolute *sine qua non*. The author feels that the relative efficiency of this drug and its methods of administration may be rated as follows:

(1) Intramuscular injection of salvarsan or equivalent.
(2) Intramuscular injection of neosalvarsan or equivalent.
(3) Intravenous injection of salvarsan.
(4) Intravenous injection of neosalvarsan.
(5) Sulpharsphenamin intramuscularly in about three times the dosage of arsphenamin.

Bismuth salts are at present in the trial stage. The likelihood of bismuth poisoning has served to lessen the earlier enthusiasm for their use.

The great drawback to the use of the intramuscular method is the severe pain at the site of injection, which incapacitates the patient for two or three days. The neosalvarsan is much less painful than the salvarsan. Either of them may be suspended in a solution of a neutral oil, such as oil of sesame. If iodopin (which is a mixture of oil of sesame with iodin) is employed, the injection can readily be prepared by anyone, without preliminary sterilization. It should be rubbed up in a sterile mortar, drawn into a sterile syringe with a large caliber needle (No. 20), gently heated, and injected. One-half of the dose should be injected into each gluteal region close to the mid-line. Despite the drawback of pain, the eventual result is so much better that in refractory cases its efficacy more than counterbalances the discomfort. The part should be vigorously massaged immediately after the injection and thus much discomfort is eliminated. Furthermore, the dose does not require frequent repetition, as is the case when the intravenous route is employed. Where less intensive measures are required ampules of salvarsan or neosalvarsan may be readily obtained, containing 1 decigram (1.543 grains) of neosalvarsan, made up with a neutral oil, which may be injected weekly exactly as mercury salicylate injections are administered; they are not much more painful than the mercurial injections, and are very satisfactory.

ARTERIOSCLEROSIS.—In all cases of valvular disease associated with high arterial tension, small doses of **mercury** with **potassium iodid** should be administered in addition to dietetic and hygienic measures. In refractory cases of undoubted rheumatic mitral disease, wonders are sometimes wrought in this way. It is in these refractory cases, as well as in all the cases which are not clearly and definitely luetic, that the older specific remedies are especially indicated. Without a definite luetic history or a positive Wassermann, one would be loath to give an intravenous injection of salvarsan. In using potassium iodid and mercury in cardiac cases, the initial doses should be very small, two grains (0.130 gram) of potassium iodid, and 1/32 (two milligrams) of bichlorid or its equivalent three times a day, gradually increasing up to ten grains (0.65 gram) of potassium iodid and 1/20 grain (three milligrams) of bichlorid of mercury three times a day; or calomel, gr. 1/10 t. i. d., may be substituted for the mercurial. Sometimes tablets of gray powder, 1 grain (0.065 gram) t. i. d., are efficient. In administering these agents, the startling results so commonly following their use in syphilis in other parts of the body are rarely in evidence. Except for the relief of pain, which the iodid so commonly accomplishes, little appreciable result is apparent until after a month or two of treatment, sometimes not until a month or two after the drug has been discontinued. A good rule in all valvular lesions is to include small doses of mercury in the interim tonics so frequently necessary in managing these cases. However, if the primary disease is luetic, once there has been a decided break in compensation little permanent improvement will follow the use of any of the antiluetic remedies. They should, nevertheless, always be diligently tried in the hope of producing a cessation of the process. Here even greater caution should be employed in the size of the initial dose. In the presence of edema, salvarsan should not be used.

ANEMIA.—Most of these patients are pale, and frequently show a true secondary anemia. Iron and a tonic, particularly arsenic and mercury, as in the following prescription, are necessary from time to time:

℞ Hydrargyri chloridi corrosivi	grain i (0.065 gram)
Liquoris potassii arsenitis	fʒiss (5.85 c.c.)
Tincturæ ferri chloridi	fʒiiiss (13.6 c.c.)
Acidi phosphorici diluti	f℥i (31.1 c.c.)
Syrupi limonis	q.s. ad f℥iv (124.40 c.c.)

Sig.: fʒj p.c. in water.

If this is not done, these patients lose their energy from time to time. The blood examination seldom reveals any satisfactory results from the administration of such hematic tonics, but symptomatically the patient is better. In some cases Fowler's solution alone is better borne.

The treatment of these minor symptoms will be discussed in detail under the treatment of individual symptoms. However, in patients presenting such minor symptoms, in spite of the fact that there is no direct or specific indication for the use of digitalis, small doses of the tincture from five to ten minims (0.3 to 0.60 gram) three times a day, continued for several weeks, will, in addition to the other measures, often make the difference between success and failure in treatment. After the relief of these symptoms a general dietitic and hygienic future course must be planned.

Such patients should not take part in any activities which induce the slightest possible shortness of breath. It may be argued that it is only by exercise that physiological hypertrophy is induced, and this might have some foundation if there had been no evidence of deep muscular damage. Once symptoms have appeared, the ordinary duties of a quiet occupation furnish sufficient muscular stimulus for the average patient; for this reason, if the family has been living on the top floor of an apartment house, the ground floor, or at most one flight up, should be taken. Curiously enough cardiac patients seem to have a fondness for a top floor. In a private house the bedroom should not be more than one flight up.

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

ALTITUDE.—These patients may usually safely go to an altitude of two thousand feet. After three thousand feet great precaution should be exercised and at the first onset of symptoms the patient must seek a lower level. As a rule individuals with cardiac involvement do better at the sea level, but not near the seashore.

CLIMATE.—Old people will always find that their heart attacks will be less frequent in a warm climate during the winter than in a cold climate. Where the financial conditions permit, cardiacs should be informed of the benefit of climatic therapy. It may often add years to the patient's life, by avoiding the cold winters with their attendant frequent head colds.

MARRIAGE.—Unless there is marked evidence of decompensation, there is no contra-indication to marriage on the part of men, with the possible exception of those suffering from aortic regurgitation. The occasional occurrence of death during the sexual act in such patients should always be borne in mind.

In the case of women, marriage is contra-indicated only because of the danger resulting from pregnancy and labor. It is quite true that many women who suffer from minor symptoms associated with mitral regurgitation do have large families with little or no serious inconvenience, yet there is always considerable risk. The well-marked cases of primary mitral stenosis are, however, nearly always bad risks because of the likelihood of the occurrence of sudden pulmonary edema during pregnancy.

The chief points of value in estimating the likelihood of the heart being able to meet the demands of pregnancy are (1) the history or absence of the occurrence of a previous loss of compensation; (2) how the heart responds to the demands of ordinary life; (3) whether or not the patient has frequent infections and a disinclination for ordinary exercise; (4) whether there is a difference of more than ten beats in the pulse frequency when the patient is in the horizontal and upright posture; (5) the relation of the urine output to the intake. Even if one points out these dangers, it seldom prevents matrimony, either because pregnancy seems far off to the prospective bride, or because she wishes someone to take care of her when the illness due to her heart attacks her. Practically, marriage does add years to the life of many such women, who otherwise would have been compelled to do hard work with no periods of rest and with exposure to infection thus bringing on an early decompensation.

What should be one's attitude when pregnancy has taken place in a patient who presents some of the minor symptoms of broken compensation?

In general the outlook is infinitely better than the symptoms seem to warrant, and most patients pass through their first pregnancy satisfactorily. If there has been a decided break in compensation, nature usually produces a spontaneous abortion. In the first group mentioned one should wait until the sixth month of pregnancy, when, if there has been no decided loss of compensation, the patient should be kept under very close observation, mostly in bed, until the end of pregnancy. If at the sixth month unmistakable symptoms of failing compensation are in evidence—not the slight edema of the legs so common in most pregnant women, but a general anasarca and dyspnea—then labor should be induced. At any time the onset of pulmonary edema demands active treatment, but labor should not be induced before the edema has subsided. Casualties usually occur with the second and third pregnancy.

TOBACCO.—The use of tobacco should be restricted. It cannot be said that the use of a small amount is uniformly bad, but unquestionably excessive smoking in the subject of high blood-pressure is often productive of harm; therefore the cardiac patient must be taught to look forward to the gradual elimination of the use of tobacco. It should be impressed upon him that he must visit the physician on a regular specified day every two or three months for re-examination.

Outline of Treatment When Minor Symptoms Have Appeared

1. General directions as given in outline on p. 166.
2. Absolute rest in bed for at least three days. Relative rest for a few weeks thereafter. An extra hour of sleep each night for the rest of life.
3. Change of occupation if symptoms are due to overwork.
4. Life on level ground—avoidance of altitude above 3000 feet—and warm climate, if possible.
5. In general, marriage to be avoided.
6. Restriction of tobacco and coffee.
7. Active treatment of cause underlying lesion. Occasional courses of small doses of potassium iodid and mercury, in all cases in which there is a definite indication for its use, as well as in refractory cases, due to any cause
8. Small doses of digitalis for two weeks to be repeated later.
9. Treatment of special symptoms:
    - (*a*) Stomach
        - Dry diet.
        - Avoidance of foods producing flatulence, such as cabbage, beans, etc.
        - Fresh fruits.
        - Fats.
        - Eggs.
        - Cheese.
        - The home use of alkalis, and carminatives, such as bicarbonate of soda, peppermint, etc., on the first appearance of flatulence.
    - (*b*) Nervous symptoms and distressing sensations about the heart.
        - Bromids.
        - cratægus (fluid extract, ♏ xx t. i. d.).
        - Hoffman's anodyne.
    - (*c*) Chest pain
        - Counterirritants.
        - Iodids.
        - Nitrites.
    - (*d*) Lungs
        - Local treatment of nose and throat.
        - Creosote.
        - Codein.
10. A course of Nauheim baths or any other safe treatment which forms an excuse for a regular vacation period.
11. After disappearance of symptoms patient to report to physician at least every two months for physical examination.

INDIVIDUAL SYMPTOMS AND THEIR TREATMENT

Shortness of Breath.—Among the early symptoms, shortness of breath is easily the most common. This is present only on moderate exertion and is similar to that experienced by any one who carries out some unaccustomed exertion, except that it is more easily induced than is normally the case and persists longer. It is essentially different from the dyspnea of the later stages of the disease and is a valuable warning. It may be in the form of frequency of respiration (polypnea) or difficulty in breathing (dyspnea) or may appear only when the patient lies down, so that he is forced to sit up to breathe (orthopnea).

The only treatment lies in prevention, i.e., the cultivating of the mental attitude that will act as an antidote to hurry and to extra effort. Dyspnea, as well as most of the major symptoms, such as pain, cough, flatulence, etc., are worse if exercise of any kind is indulged in within half an hour after a meal.

When this shortness of breath becomes evident on slight exertion, small doses of **digitalis,** given for a few weeks, are of undoubted value, after which time the patient is apparently as well as ever. But recurrences will take place and they are to be managed along the same general lines.

Weakness.—As a symptom of chronic heart disease weakness is perhaps the most common early manifestation. The consciousness of failing power, and of inability to perform ordinary avocations, or the necessity of putting out of greater effort than usual in doing so, impresses itself on the patient's mind long before the ordinary objective signs of heart disease are manifest. Almost everyone with a rapid pulse of long standing, from any cause whatever, complains of weakness as a presenting symptom. If the patient does not volunteer it, one may, in any disturbance of cardiac compensation, affirm that weakness is present. It is an end-of-the-day symptom, and is often associated with breathlessness on exertion. Breathlessness and fatigue in the old are almost always cardiac phenomena. Weakness in cardiacs sometimes occurs during the early morning hours and is apt to be confusing. This is often due to an intercurrent endocrine disturbance and not to the heart itself.

Closely related is the so-called effort syndrome. Here, aside from subjective disturbance of a very rapid heart, weakness is the outstanding symptom. The fact that true weakness is always present in heart disease itself will often make for confusion. The other symptoms of the effort syndrome, together with the inability to find a cardiac defect, will serve to solve the difficulty. No one with true organic disease of the heart could suffer the amount of cardiac distress such as these effort syndrome patients have, without showing some defect on careful examination.

The first or organic group of those suffering from weakness may be differentiated from the effort syndrome cases (1) by being a late-in-the-day symptom, whereas in the second or so-called functional group weakness is almost always a morning symptom; (2) its lack of boostability (to coin a word). In the functional group it is almost always possible to boost the patient by excitement, which enables him to carry on, whereas in the organic group this is rarely possible; (3) the appearance of the patient confirms one in the opinion as to the relative innocuousness of his complaint. In the functional case it is usually difficult to reconcile the appearance of the muscular development with an organic cause as a basis for the complaint; (4) the presence of associated symptoms. Various neurasthenic symptoms, as dizziness, head discomfort, etc., are regularly present in the functional case. It is true that they are at times present in the organic case, but not so regularly as is the case in the one suffering from the functional disturbance; (5) the presence of a large or moderately large heart speaks for organic changes as the cause. It must always be kept in mind that it requires little to produce weakness in one who is already suffering from an organic disease or even from a well-established functional disturbance.

Treatment.—In the first group, (1) attempts as far as possible to get rid of the cause, (2) absolute rest in bed at first; this is to be followed by cautious partial steps in getting out of the bed, staying up for a half hour, then an hour, and so on. Great care must be exercised that the patient does not overdo himself. Any severe exertion is very apt to start up the whole trouble worse than before; (3) tonics and restoratives, especially strychnia, in the uncomplicated cases; (4) adjuvant measures to support the patient; an abdominal belt or bandage is generally necessary.

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

The principle of this belt is that it acts as a tonic to the abdominal or solar plexus, so that whenever a patient who has been in bed convalescing from an acute disease attempts to get up and walk, one should put on an abdominal bandage made of a towel, or other material, pinned tightly about the abdomen; later on a more elaborate abdominal bandage may be ordered. Most physicians are familiar with the feeling of faintness that such a patient experiences when she suddenly gets up for the first time; this bandage prevents this accident. Strips of adhesive plaster, three inches wide, across the abdomen is a handy way of testing its value or necessity.

Place of Alcohol.—In many of these cases, both heart and post-infectious types, alcohol given with the meal, or with milk between the meals, is a sovereign remedy. This is especially true of the aged. Digitalis in small doses in old cardiacs is of service, but slow in showing results. Iron does have some tonic and recuperative powers; a pill containing iron and strychnin is an old favorite.

Excepting in the cases associated with convalescence from acute disease or anemia, no quick and permanent change can be effected in any patient whose chief complaint is weakness. It is a symptom of grave importance, if one excepts the acute cases and those due to nervous disease. In any event one can prognosticate that it will take a long time for recovery.

Dyspnea.—The dyspnea of the later stages is essentially different from that which appears before the break in compensation. Now the patient becomes dyspneic without any exertion, and at the most unlooked-for times. It is present soon after falling asleep. However, it is usually in the early morning hours that this symptom is most troublesome. He cannot sleep because of this dyspnea, or if he does fall asleep, awakes with a gasping; this is so disagreeable that he is afraid to go to sleep again, and this makes matters worse. At other times he becomes dyspneic during the day, without appearing to notice it. Occasionally a hypo of M V of adrenalin is successful in permitting the patient to fall asleep.

The Cheyne-Stokes phenomenon, either partial or complete, is present in nearly all those who have high blood pressure, and in a large proportion of the others who have had several breaks in compensation. It is frequently present for a year or more before death. This is especially so during sleep and becomes noticeable only when observed during waking hours. Commonly the patient himself does not recognize it. A somewhat similar type of breathing occurs long before the well-marked Cheyne-Stokes phenomenon is evident. After the summit of the curve of frequency of respiration is reached, respiration suddenly stops, and the gradual decline of Cheyne-Stokes is missing.

There is no specific treatment for this form of dyspnea. It is simply an index of the progress of the disease. When it becomes severe enough for the patient to appreciate it and suffer as a consequence of it, complete recovery is a rarity, yet it may apparently improve for a considerable period of time.

For individual attacks of dyspnea, **Hoffman's anodyne** in ½ dram (1.95 c.c.) doses repeated every hour or so is often efficacious. It should be given in sugar and water. However, it soon loses its effect, and the abnormal respiration continues even in spite of large doses of digitalis. Then **morphin** is our only recourse. Generally it is necessary to give it hypodermically in order to obtain prompt results.

In the administration of morphin there is much fear among the profession that the patient will forget to breathe or that the medullary center will not respond to the increase in carbon dioxid when it is benumbed by the narcotic. Of this there need be no fear. On the other hand the terror of the dyspnea, and the sleeplessness which results will do much to still further break down the compensation, unless sleep is secured.

At times, **atropin,** grain 1/100 (0.00065 gram) or larger doses at bedtime, by hypodermic, will control the attacks, and should be tried.

On occasion we have seen a dry carbon dioxide bath afford relief, but the mechanism of giving such a bath of the gas itself is too cumbersome for extended use. On the other hand the administration of oxygen, especially after the manner suggested by Meakins, is of great usefulness. It must be admitted that it is only a temporary measure, but the relief afforded is often sufficient excuse for its use. Instead of the traditional funnel a Y glass tube is inserted in the tube leading from the container, and the ends of two small catheters are inserted onto the two ends of the Y tube, and placed within the patient's nostrils; then the oxygen is turned on for fifteen minutes, and off, and so on. By this means one does secure considerable relief from the dyspnea.

Dropsy.—Rest in bed is the best general measure for the treatment of this condition. Most of the early cardiac dropsies disappear when the patient remains in bed for three or four days, only to return when he gets up.

In those patients who insist upon getting about, and who are suffering from a slight dropsy that is only noticeable at the end of the day, the application of a bandage in the morning—from the feet up to the knees—and the addition daily of an extra hour in bed, is a practical temporary measure.

When the dropsy becomes severe, other measures must be employed in addition to rest in bed. Of these, **digitalis** easily takes first place.

Cardiac dropsy is the red light pointing to right heart failure, and digitalis is always indicated in right heart failure, no matter what the cause may be. It has an especial predilection, however, for the right heart failure consequent on rheumatic disease.

Sometimes the drug is not active until the abdominal cavity or a pleural transudate is relieved by paracentesis. At other times it is effective only after active purgation.

If no results are obtained in three days, one should change the digitalis preparation employed. A **Niemeyer pill,** 1 grain each of powdered digitalis, squills and calomel, given under these circumstances has often made the reputation of a consultant. One pill three times a day for not more than three days should be ordered. This limitation should be a standing order, because these patients are easily salivated. A single dose of **calomel,** gr. 1 or gr. 2, and **compound jalap powder,** 1 dram (1.95 grams), is generally indicated at the beginning of treatment, but active continuous catharsis given with the idea of reducing edema is seldom well borne. In the few cases in which good results follow the purgation, the jalap powder or **elaterin,** grain 1/6 (0.0108 gram), repeated daily, are efficient. Commonly it will be found that after the first dose active catharsis does not avail much for the relief of dropsy. **Hot baths** and **hot packs** are of value when there is coincident renal disease, but one must be very careful during the administration of the first hot bath or pack, because some cardiac patients become very much cyanosed while in the bath. If this does not happen, it is likely that the baths are efficient for that individual. Pilocarpin should under no circumstances

PRACTICE OF MEDICINE—TICE

Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

be employed, as it frequently produces pulmonary edema in cardiac patients.

A very useful method of relieving edema of the extremities is by means of incision, or drainage. The amount of fluid that can be so removed is often prodigious; as much as a half gallon in one day is often obtained. Commonly there is much hesitancy in resorting to this procedure, and it is usually done only at the consultant's direction in advanced stages of the edema. The fear of injury of the patient, and of sepsis, act as barriers in the minds of most physicians. There is practically no pain, as the tissues are so much distended as to be almost anæsthetic, and the danger of sepsis with ordinary care is very slight.

Instead of either incision or of Southey's tubes, which almost no practitioner possesses, the insertion of a half dozen aspirating needles of twenty gauge, or larger, and the surrounding of the open ends of the protruding needles with a boric acid gauze, is all that is necessary. They should be plunged into the limb in the direction of the heart, and should penetrate from ⅛ to ½ inch. If need be, simple puncture is often quite efficacious.

Pulmonary Edema.—Pulmonary edema is a frequent symptom in the course of valvular disease. It is especially frequent in aortic disease. Attacks much like those of acute suffocative pulmonary edema so common in aortic disease occur in the primary form of mitral stenosis. Here they usually follow some violent exertion, as skipping rope, running up a flight of stairs, etc. Occasionally such a patient drops dead during the exertion, but the occurrence of an attack of pulmonary edema is more common. There is great oppression in the chest, rapid irregular pulse, frothy pink expectoration, and often bleeding from the nose or mouth. Such attacks are responsible for the commonly accepted theory that death and broken compensation are directly due to effort. As a matter of fact such an attack of pulmonary edema is comparatively rare. The attack lasts from one to two hours, and within a day the patient is normal again except for a headache and sense of weakness. Generally speaking the prognosis is rarely as serious as it looks at the time.

These patients have many such attacks, which are often continued paroxysms of auricular fibrillation and accompanied by many hysterical manifestations.

Such a patient may have many such attacks until finally in one attack no different from the rest, the patient dies. Much adverse criticism is apt to follow if the patient has been treated as an hysteric, so that it is well to regard every attack as a serious possibility.

The treatment consists (1) in a hypodermic injection of **morphin sulphate,** grain ⅓ (gram 0.0216), with **atropin sulphate,** grain 1/75 (gram 0.000846), (2) **dry cups** applied to the base of the lungs, or in the absence of cups a large mustard plaster, (3) reassuring the patient that he or she will not perish. This statement is of inestimable value as an adjuvant in treatment. The friends should however be informed at once of the seriousness of the condition. Sometimes **nitroglycerin** is helpful, particularly if high blood pressure is present. Nitrate of amyl, the idol of the medical student, has not been very satisfactory in my experience. **Bleeding** is occasionally of service if cyanosis is very marked. If a large sized needle, such as is used for blood transfusion, is used, it may be done without getting blood over the clothing, especially if the blood is drained away through a rubber tube attached to the needle.

Cough and Bronchitis.—The earliest cough is a single effort cough.

It is noticeable only on exertion, on going out in the cold or at the beginning of a sentence. It is frequently called a stomach cough because it often comes after a full meal or during excitement. It is not troublesome and is only noticed by the friends of the patient.

Unless there is an added bronchitis, the cough itself rarely calls for treatment. Frequently it will be found that there are enlarged follicles in the pharynx—an enlarged lingual tonsil—or some congestion of the larynx. In such cases, local treatment with a two per cent. **silver nitrate** solution is often helpful.

When there is an associated bronchitis—particularly in old people—it is very resistant to treatment. Here the addition of small doses of from two to five minims (0.125 to 0.31 c.c.) of the tincture of **digitalis** to each dose of the cough mixture, containing **creosote** or a **terebene** derivative and **codein** or **heroin,** is of much value in hastening recovery. Of course if the attack is very severe, rest in bed is absolutely necessary. If there has been a previous severe break in compensation, such an attack of bronchitis should be considered just as serious as a pneumonia occurring in a normal individual.

Failure to regard bronchitis with the slighest elevation of temperature as a serious lesion in a cardiac patient is responsible for a large proportion of the deaths in such patients. The fear that narcotics will benumb the respiratory center and thus retard expectoration seems still to be favorite teaching; practically they are our most valuable aids.

Late in the course of broken compensation, the presence of cough, due to congestion of the bronchi and lungs from back pressure, is a serious complication. Each attack of coughing is as depressing to the heart as would be the running up of a flight of stairs.

This cough must be suppressed at all hazards, and codein or morphin must be given in sufficient doses to accomplish this result. Usually, codein, grain 1/4 (gram 0.0162), or heroin, grain 1/12 (gram 0.0054), or pantopon, gr. 1/6 (gram 0.0108) every three hours, is sufficient. Sometimes chloral in five to ten grain (0.324 to 0.650 gram) doses in addition to the morphin is advised. No preconceived fear as to pulmonary edema, etc., should cause the practitioner to withhold the narcotic.

Digestive Symptoms.—Almost all cardiac patients suffer sooner or later from symptoms referable to the digestive tract. Often these symptoms are treated for years on the assumption that they are due to disease of the stomach. Only a thorough examination reveals the real cause. The stomach may well be termed the red light signal station of all of the internal organs. The time of the appearance of these stomach symptoms may be divided into two periods: (1) before there is evidence of broken compensation, (2) during the period of broken compensation. At first the symptoms consist in a sense of fullness and oppression with belching coming on soon after meals, and later a sense of precordial distress, rarely of pain in the abdomen or chest. Frequently there is the complaint of pain radiating down the arm, particularly if exercise of any kind is indulged in after meals. Often it is not noticed until the patient goes out in the air.

The common gastric complaints of the cardiac patient are: pain about the epigastric region, vomiting, diarrhea, lack of appetite, constipation, belching, fullness and flatulence. These complaints are not placed in order of frequency, but for convenience will be taken up in the above order.

In discussing the relationship between gastro-intestinal symptoms and heart of a prominent citizen suddenly gives out, acute indigestion is the term that satisfies the coroner's physician. In most of the cases of cardiac indigestion stomach analysis reveals only an excess of mucus and a low HCl content.

Treatment.—The dictum that in the treatment of heart disease the treatment of the stomach and nervous systems is more successful in placing the patient on his feet than is the treatment of the heart itself, is a truism, and clinicians in general will bear out this statement.

The subject of treatment may be divided into: (1) the management of the acute attack, and (2) the sub-acute or recurring cases. In the management of the hyper-acute attack, it is well to have ready on the tip of one's tongue, to be ordered over the telephone, if need be, a regular sequence of remedial measures to be employed:

(1) A glass of hot water with one teaspoonful of sodium bicarbonate.
(2) Clove water, made by dropping a dozen whole cloves in a glass of boiling water and allowing it to stand five to ten minutes, then drink the solution.
(3) Hoffman's anodyne (always to be kept in the home of cardiacs).
(4) Aromatic spirits of ammonia.
(5) Jamaica ginger, or any household carminative.
(6) A simple soap suds enema.
(7) This prescription:

℞ Spiritus ammoniæ aromatici.............fʒiv
Spiritus chloroformi.....................fʒii
Tincturæ zingiberis.....................fʒii
Spiritus lavendulæci q.s. ad.............f℥vi
♏ Sig. fʒss every two hours.

(8) Mustard plaster over stomach.
(9) Turpentine stupes.
(10) Turpentine enema.
(11) Turpentine by mouth.
(12) Milk of asafœtida enema.
(13) Caution the patient to avoid gulping or air swallowing.
(14) Rehfuss tube.
(15) Stomach tube.

Ordinarily, in a manifestly ill cardiac, the suggestion to use a stomach tube for either persistent vomiting or for flatulence and distress will be viewed with horror. No one wants the patient to die while such an operation is being performed. The author has never seen anyone seriously injured by the performance of stomach lavage, but on the other hand, has seen relief and sleep that could not be secured by morphine. In a severe case, resisting all of the ordinary measures, it is of inestimable benefit. Auto-lavage may sometimes be practised, but as a rule the general prostration and distress following vomiting is more of a strain than the retching resulting from passing a small stomach tube. The passing of the Rehfuss tube and washing through it will sometimes avoid the use of the larger tube.

(16) Pituitrin (surgical) 1 c.c. hypodermically. If there is any reason to feel that the trouble is likely due to colon distention, a simple enema will often effect the quickest and most satisfactory relief. If high blood pressure is present, nitroglycerine, grain 1/100 under the tongue, often gives relief. It should always be tried early, in the high blood pressure cases.

Generally the clinical picture is rather that of recurring attacks, with a varying interval, until finally, in the bed-ridden patient, he suffers continually after each meal. These cyclical attacks occur with considerable degree of regularity. It is an open question whether the underlying cause is a fresh infection or whether these attacks are in the same category with other cyclical disturbances, such as migraine, epilepsy, menstruation, etc. Personally, the author is sure that many digestive attacks in normal individuals are of a cyclical nature.

In the management of recurring cases the diet is of utmost importance: (1) Dry diet—this means that these patients should not be allowed any liquids with their meals, nor within an hour after the meals. This is the most difficult rule to enforce. To secure the patient's coöperation one must explain the ptotic result of ingestion of liquids with meals. A diet list should be furnished each patient. (2) No condiments—this includes celery, radishes, etc.; flatulent foods, such as cabbage, beans, onions and bananas, are forbidden. No raw fruits, butter, fats, cream, cheese or eggs.

When milk is taken it preferably should be skimmed milk. Tea or coffee should not contain cream or milk, nor should food be taken with either of them. However, a dry roll is often permissible with coffee. Cocoa and chocolate in any form are not allowed. Soups are generally condemned. The author has found that meat in small quantities is not badly borne, provided the other rules above mentioned are followed. Many of these patients say that meat does not agree. The disagreement is most often due to (1) either too much is ingested, or (2) fluids are taken at the same time. Unless a personal idiosyncrasy exists, meat in small quantities is not harmful, provided there is not also present an advanced interstitial nephritis. A urine with a specific gravity over 1015 at all times, with a normal urea output, even though there is a trace of albumen and casts present, does not warrant any restriction in protein intake. In fact a fair, but not excessive, protein diet is indicated, and often transforms the disheartened, dejected invalid into one who can earn his living.

Cold drinks and unfermented juices must be avoided. Lemonade is a common offender. No salt should be put on the tray, especially if edema is present. No exercise should be allowed within at least one hour after meals and the meals should be eaten slowly.

A sample of allowed foods in the early stage of decompensation follows:

Liquids—Junket, milk and gruels.
Semi-solids—Arrowroot, cereals (well cooked), corn-starch, custards, milk toast, rice, tapioca, and vegetable soups.
Light Diet—Bacon, boiled fish, baked or mashed potatoes, bread, cooked fruit, green vegetables (excepting cauliflower, cabbage, radishes, cucumbers), scraped beef, small amounts of chicken or squab and white fish.
General Diet.—A more liberal selection of foods is allowed, excepting the following: Bananas, cabbage, cauliflower, corned beef, cucumbers, fried or greasy foods, hot breads, lima beans, navy beans, pastry, pork, radishes, rutabagas, spiced meat, and veal. No cake is permitted, except cakes made upon an egg foundation, as angel food, sunshine cake, lady fingers and sponge cake. In addition to this list, all foods for which there is a distaste or which cause the individual discomfort are to be avoided.
Black coffee, dry rolls, cereal.

Because of home conditions, often a diet must be constructed the preparation of which involves a minimum of labor and expense. The following schedule of diets will serve as types of easily prepared foods:

Breakfast: Oatmeal, or other cereal, glass of skimmed milk.
10 A.M.: Oatmeal gruel, prunes.
Dinner: Ground beef steak, baked potatoes, prunes or baked apple.
2 P.M.: Oatmeal gruel, black tea.
Tea: Toast, prunes, baked apple, milk, milk at bedtime.
Breakfast: Dates, rice, prunes, toast, milk, 10 A.M.
Dinner: Baked rice, toast, butter, apple sauce, 2 P.M.
Supper: Mashed potatoes, bread, apricots stewed, graham bread and butter.
Breakfast: Stewed figs, Pettijohns, or other cereal, hot milk.
10 A.M.: Gruel.
Dinner: Broiled fish, mashed potatoe, prunes.
2 P.M.: Gruel, rice or panada.
Supper: Lettuce sandwiches, blanc mange, milk.
Breakfast: Apricots, cream of wheat.

PRACTICE OF MEDICINE—TICE
☛ **Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.**

10 A.M.: Cream of wheat gruel.
Dinner: Baked rice, prune sauce.
2 P.M.: Cream of wheat gruel.
Supper: Whole-wheat bread, rice pudding, milk, panada.

It will be noted that not much attempt is made to approximate the number of calories that are requisite for a healthy man. If the appetite is present and the food agrees, the quantity may be increased to the point of satiety; but the rule " No appetite, no food " should be insisted on, as otherwise digestive upsets are the rule.

On the occurrence of edema the same foods may be allowed, but salt must be interdicted. At first it must be removed from the tray and later from the food entirely. Under such conditions a restriction of fluids to 28 oz. a day is the first step. Milk constitutes the best food, and a diet confined to a restricted amount of milk is termed a Karrell diet, although this restriction was probably in use in one form or other since the days of Hippocrates. After the disappearance of the edema one may gradually increase the amount of fluid and solid up to the first suggested diet. It is always better to give five small meals rather than three large ones. If there is much disgust for milk, it should be mixed with gruels, cereals, malted milk, vichy, etc. Whiskey between meals often nourishes and transforms the slough of despond of the cardiac into a realm of superiority and satisfaction. In every case not readily responding to treatment, the colon must always be viewed as a likely cause of the distress, and above all else, constipation must be avoided.

The first thing to do for the recurring attacks of flatulence is to administer a dose of castor oil; no other agent acts quite so well in temporarily ridding the bowels of gas. In some patients a daily enema is satisfactory. Others are much prostrated after enemas. Care should be taken not to use a flatulent cathartic, such as magnesium citrate. Thin cardiacs bear salines badly; in plethoric patients they do well. As a rule, for continued use, one of the vegetable cathartics, as cascara aromatic, every evening after supper is preferable. As a matter of fact death at stool is a common form of death among cardiacs.

If high blood pressure is present, a bi-weekly dose of castor oil is better as a cathartic, provided prostration does not follow. Occasionally, however, such a patient is much prostrated by its use. Attention should be given to nose and throat. In cases where digitalis is indicated, after digitalization has been accomplished, medicines of this series should not be given in more than two daily doses. Opiates, when indicated, are best combined with a laxative, such as

℞	Tr. opii deodorati	fʒiss (6.00 c.c.)
	Fl. ex. cascaræ aromaticæ	fʒiv (16.00 c.c.)
	Elix. adjuvantis, q.s. ad	f℥ii (64.00 c.c.)
M	Sig. fʒj b.d.	

In all cases, during the cycle of the attack, an alkali, either in the form of sodium bicarbonate, gr. x, or magnesia, gr. x, or both, should be given half an hour after meals and at bedtime, as follows:

℞	Natrii bicarbonatis	ʒiv (15.50 grams)
	Magnesii ustæ	ʒiii (11.05 grams)
	Caryophylii olei sal	ʒii (7.75 grams)
M	Sig. fʒj one-half hour p.c.	

The rationale is the same as in any disturbance of stomach motility. It causes the opening of the pylorus. In spite of the low acidity present hydrochloric acid has not been serviceable in the author's hands. Inasmuch as hyper-excitability of the vagi is responsible for so many cases wherein one cannot incriminate the faulty motility as being due to either abdominal pathology or faulty food, it is good practice in such cases to begin with a course of bromid: 20 to 30 grains of bromid of soda in cinnamon water and milk of magnesia, after meals. This is generally a good routine prescription. The author would suggest this prescription as a refuge for the dispensary physician when he has not time to unearth the cause of the flatulence, rather than the routine use of the rhubarb and soda mixture, which is so commonly prescribed under such conditions. In other instances the following prescription has served the author well, especially when epigastric pain was complained of:

℞ Chloral hydratis.............. ....ʒiss (6.00 grams)
Sod. hyposulphitis....... ....ʒii (8.00 grams)
Aq. menth. pip. q.s.ad. .. ..f℥ii (64.00 c.c.)
ɱ Sig. fʒj a.c. in water.

In all high blood-pressure cases where the flatulence comes on shortly after getting up from the table, 1/100 gr. (0.00064 gram) or less of **nitroglycerine** should be given immediately after the meal, and before the patient gets up from the table. High colon enemas are frequently prescribed for patients suffering from high blood pressure and are often well borne and are followed by much relief, but if cardiac decompensation is present they should be administered cautiously and discontinued on the appearance of prostration. From time to time carminatives, such as asafœtida, ginger creosote, peppermint or oil of cloves, must be employed.

Many of these patients suffer from a potential visceroptosis, which becomes troublesome only during the cycle of the attacks. The loss of weight in cardiacs emphasizes this ptosis. In a very large proportion of cases the application of two or three strips of wide adhesive plaster across the abdomen is of utmost service. The use of plaster in this way is often one of the most satisfactory procedures in the management of these patients. This is particularly true in long-waisted people. Inasmuch as patients are fairly free from symptoms between attacks, this may avoid the purchase of an abdominal support. The peroxides of magnesium have not been successful in relieving gas in the author's hands.

In the severer types of digestive symptoms, such as are met with in bed patients suffering from broken compensation, the sufferer often feels better for half an hour or more after each meal, in which case he should be fed often and in smaller quantities.

Frequently this belching is promptly relieved at the time by the use of Hoffman's anodyne, in ½ dram (1.95 c.c.) doses, repeated as required.

Other carminatives, such as cloves, ginger, and peppermint, must be tried from time to time.

Acute dilatation of the stomach is not infrequent, and is a serious problem. In such cases there is repeated belching, swallowing of air, vomiting of small amounts of dark colored material, much fullness and distention of the abdomen, and oppressive dyspnea. The patient cannot lie down nor remain in one position for more than a few moments, and his distress is extreme.

If Hoffman's anodyne and the alkalis do not give relief, the practitioner's next thought is to resort to **morphin**, but he will often be disappointed because after two or three injections no relief is obtained.

This is one of the very few cardiac complications which are not relieved by morphin. Under no circumstances should the doctor leave such a patient until he is relieved. When all of the usual remedies have been

PRACTICE OF MEDICINE—TICE
☛ **Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.**

employed in vain, then the best remedy is the **stomach-tube, and lavage.** This suggestion appalls most physicians, who fear that the straining of the patient while swallowing the tube will be sufficient to produce unfavorable or fatal results. However, as a matter of fact, there is no danger, and after the procedure is finished the patient is usually relieved and goes to sleep. It is a sovereign remedy, and many patients die because it is not employed. The Rehfuss or any other duodenal tube is easily swallowed, and is a great improvement in the treatment of this symptom. It may be left in for an hour or more. When the symptom is very severe, pituitrin (obstetrical), 2 c.c. (32.4 minims), given hypodermically every two hours is of service. Abdominal massage is often of some help.

Vomiting.—Occasional vomiting is fairly frequent, and demands no treatment except starvation for a day or two, and regulation of diet. When it is persistent, medicines administered for the disease, such as digitalis, etc., should be considered as the most likely cause. After the discontinuance of the medicines, gastric sedatives such as bismuth, or cerium oxalate, should be employed. The following prescription is often efficient:

℞	Bismuthi subnitratis	grains viii (0.52 gram)
	Natrii bicarbonatis	grains v (0.324 gram)
	Hydrargyri chloridi miti	grain 1/6 (0.0108 gram)

M̄ Sig. One powder every three hours for four doses.

If much pain or distress codein sulphate, grain ½ (gram 0.032), is to be added to each dose; rarely nitroglycerin, gram 1/200, is to be added. Ice is seldom of avail and often increases the flatulence which so commonly is already present; absolute starvation for a day is frequently necessary. If these measures fail, or if there is evidence of a chronic gastric catarrh, **tincturæ capsici,** one minim (c.c. 0.067), before meals in a wine-glass full of water is often successful; small doses of **chloral**, grain ii (gram 0.12) to grain v (gram 0.3), every three hours is often of service. **Ipecac** in homeopathic doses may succeed when all else fails; likewise several doses of ipecac are often successful. If all of these measures fail, the stomach tube should be fearlessly employed, because if this vomiting is not stopped promptly it is apt to have a fatal ending. At all events it is a serious symptom if it is due to the heart itself.

Diarrhea.—Diarrhea is sometimes a distressing feature. It is often difficult to deal with. It is due to (1) the ingestion of faulty food, (2) to drugs, (3) to toxemia of the disease itself, (4) to the faulty elimination of kidneys. A dose of castor oil and starvation with stopping of medicines will eliminate the first two causes, a study of the urine and blood will determine whether (3) or (4) is responsible. Of course if it be an attempt of nature to eliminate toxins, one must be slow in stopping it. Either morphin, gr. 1/6 (gram 0.012), or tannigen, gr. x (gram 0.6), every four hours, or both, will usually stop a diarrhea due to cardiac disease.

Lack of appetite is usually nature's warning that food cannot be satisfactorily handled. A bitter, such as compound tincture of gentian or the rhubarb and ipecac mixtures before meals, sometimes causes the patient to relish his food. In general it is believed that the lack of appetite is a conservative process and should be left alone.

Other uncommon symptoms, such as thirst, are sometimes classed as due to digestive disturbance. Thirst is often closely related to hunger, in that the patient feels like taking something for the " all gone " feeling.

It is often due to an associated renal disease. In a seriously ill cardiac, persistent thirst is a bad omen.

Hiccough.—Hiccough is a very distressing symptom. It is usually manifest only in advanced cases, and in itself aggravates the patient's condition. The cardiac patient is just as apt to develop epidemic hiccough as others. The association of such hiccough with influenza will always serve to differentiate it from ordinary hiccough. It is very difficult to control, and if it is long continued recovery is uncommon. The ordinary household maneuvers should be employed, such as holding the breath, taking long breaths, holding the tongue out of the mouth, etc. A measure sometimes of service is placing a spoon on the tongue and depressing it so as to push the tongue far back in the throat and holding it there; occasionally pressing the eyeballs, straining and many other maneuvers have all at times been successful; spraying the throat with **cocain** and **adrenalin** solution will often give relief.

The stomach is responsible for a fair percentage of these cases, and through this the reflex of the phrenic is disturbed. The patient should be starved for twelve hours, no liquids being allowed. From time to time aromatic spirits of ammonia and Hoffman's anodyne should be given. These failing, a mustard-plaster over the epigastrium may afford relief. **Chloral hydrate,** in 10 grain (gram 0.6) doses, sometimes relieves. Sometimes taking a food or medicine which is strong, bitter or sharp in taste stops the paroxysms. **Benzyl benzoate,** ½ dram (1.9 c.c.) of a twenty per cent. solution or emulsion repeated every three hours, is efficient. It has no toxic effects, but is unreliable. The same is true of the much vaunted musk.

Finally, when they are long continued, rest must be obtained by the use of morphin, although frequently it does not prevent the occurrence of the hiccough during sleep. One must keep on trying one remedy after another, inasmuch as in all hiccoughs the psychic effect of a new remedy is always a powerful adjuvant. The author has not been able to convince himself that any of the remedies directed toward influencing the phrenic nerve itself have been specifically efficacious.

Insomnia.—Sleeplessness is one of the earliest of the minor symptoms to appear. The patient seldom complains greatly of it, because of the insidious onset. It is the worst of the minor symptoms because it is constantly wearing out the patient's reserve power. More than any other symptom, with the possible exception of pain, it must be overcome. This applies in all stages throughout the life of the cardiac patient. In these early cases a glass of hot milk or cocoa is sometimes sufficient to induce sleep; in others, a glass of hot rum, whiskey or a bottle of beer is sufficient, but in nearly all instances this habit of sleeplessness—for this it soon becomes—cannot be broken except by the use of drugs. There is often disinclination on the part of the doctor to use drugs for this insomnia, and on the part of the patient and his friends a tendency to charge up any mental depression to the remedy employed. Of course all cardiacs do have fits of mental depression; especially is this so at the very time that it is necessary to give medicines for the heart itself. The author has never seen any decided mental depression following upon the use of cardiants.

In the early cases, sodium or potassium bromid in twenty grain (1.30 grams) doses, three times a day and at bedtime for three days, and after that at supper and bedtime, is sufficient to bring about natural sleep. There is no special value in the mixed bromids. In other cases, chloral

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

in fifteen grain (0.972 gram) doses after supper and at bedtime is necessary. The elixir of chloralimid in half-ounce doses at bedtime is safer and generally efficacious. In the more advanced cases, veronal, in ten grain (0.65 gram) doses in hot milk, repeated in three hours if needed, is often successful. Luminal, in from three to five grain (0.195 to 0.324 gram) doses, is often more successful than veronal.

Among the newer drugs, allonal, combining as it does a pain-relieving agent with a soporific in one dose, is fairly efficient. It may often be quite well substituted for bromid as a regular sedative. The dose is one tablet (2½ grains) twice or three times a day. Four tablets is a safe limit. Neonal is the latest addition to the list of hypnotics for cardiacs.

If the major symptoms are present, it is usually necessary to resort to morphin in order to secure a few nights' sleep, as these milder agents are now inefficient. For the first few nights it should be given in doses of 1/6 to 1/4 grain (0.0108 to 0.0162 gram) hypodermically. Its action by mouth is slow and not nearly so satisfactory. If no effect follows within half an hour after the hypodermic, it may be repeated. The oral administration of the narcotic should not be repeated within two hours.

Headache.—Headache is frequently temporal, occasionally frontal. When due to intercurrent causes, such as eye-strain, constipation, etc., it should be treated on the basis of the intercurrent cause. Frequently, tying a handkerchief about the head gives much relief; in aged people an old-fashioned nightcap is often comfortable. One should always strive to learn if the headache is due to the cough that accompanies an intercurrent head cold, and if so to treat accordingly; cough headache is to be combated by codein or heroin, with or without chloral, in the last resort chloral or morphin.

When it can be attributed to the cardiac disease, rest is of immediate importance. A powder containing phenacetin, grains five (0.324 gram), or aspirin, grains ten (0.65 gram), with or without guarana, five grains (0.324 gram), is a safe and satisfactory agent. The author does not find that the average cardiac patient is any more prone to cyanosis and cardiac distress after moderate use of these remedies than is any other class of patients.

There are always some people who are susceptible to the coal-tar derivatives; but the condition of the heart, as far as can be found on gross examinations, has little to do with this idiosyncrasy. The cyanosis is often a question of blood chemistry rather than of cardiac insufficiency.

When the headache is frequent and continuous, a treatment of the cause underlying the cardiac lesion by digitalis, iodid or nitrite is commonly satisfactory. In cases associated with high blood-pressure bromids are often of value. In the severer cases, venesection (a pint of blood being withdrawn) frequently relieves the headache for several months. This failing, absolute rest in bed should be insisted upon. One should try these measures in their successive order, and if they fail morphin is an unfailing source of temporary relief. Lumbar puncture may rarely be employed as a last resort, but it is occasionally dangerous in cardiacs.

Delirium.—The delirium and mental aberration that is present in most cardiac patients during a severe loss in compensation is the cause of much alarm to the friends of the patient. While it always has a serious portent, yet, in the absence of other signs of progressive disease, it is not necessarily fatal. When it continues for several days the question is frequently asked: Will the patient be permanently insane? In general a positive statement can be made as to such an outcome. It is very rare that these patients actually become insane. Here again one must closely distinguish between an insane person who has a cardiac lesion and one who is suffering from the delirium of decompensation.

As to the cause of these mental changes—the laity almost always believe it to be due to the medicine prescribed, particularly if morphin has been given hypodermically. On the other hand, many physicians believe that digitalis is responsible for the delirium.

Except in the rarest instances neither of these views is correct. It is an unquestioned fact that digitalis has, in very exceptional instances, when given in very large doses, produced this phenomenon. But this is exceedingly rare. The same holds good to a lesser degree as to morphin, whereas delirium is a common phenomenon in all cardiac patients.

When there is much adverse criticism it is a good practice to stop all medicines for a day or two unless there is dire necessity for their use. The continuance of the symptoms will be convincing. Of course the symptoms stop at times of themselves, but usually they return.

As to the treatment: A hot pack is frequently serviceable. Bromids are useless. Paraldehyd in 1 dram (3.75 grains) doses is a safe agent. At times it may be increased to 2 drams (7.80 grams) every three hours. Chloral in from fifteen to twenty grain (0.97 to 1.30 grams) doses is a valuable agent and is practically devoid of danger within these dose limits. Veronal in ten grain (0.65 gram) doses is safe but is not as reliable as it is in delirium due to other diseases. Luminal is more often serviceable, and is given in doses of from three to five grains (0.195 to 0.324 gram). Occasionally it produces a severe urticaria.

Cardiac Pains.—Pain in the region of the heart is so frequently due to causes other than the heart that it has become almost an axiom that in the presence of precordial pain, the heart is the last place in which to look for the cause. Yet this is only relatively true. Most cardiac patients do have pain about the heart at some time. One must distinguish between discomfort and a sense of weight and actual pain. If the pain is continuous, and there are other evidences of cardiac disease, the cause is almost certainly in the heart, whereas if it is paroxysmal and no cardiovascular symptoms are evident, the cause is likely to be found elsewhere.

Where the disease involves the base, it involves the reflex arcs of the cervical and thoracic nerves. In the great majority of cases the pain is referred under the left breast and across the mid-chest. It commonly radiates down the inner side of the arm to the little finger. Often hyperalgesia is also present.

Other thoracic pains are due to pulmonary infarct, pleurisy and pericarditis.

Pain in the epigastrium in cardiacs is usually due (1) to dilatation of the right heart, (2) to congestion of the portal system, and (3) to enlargement of the liver. Nearly all decompensating cardiac patients have pain, tenderness or uneasiness in the epigastrium. The relief of this pain follows in proportion to the relief of its cause. It is seldom agonizing, but is constant and annoying.

Local Treatment.—By the use of counterirritants over the heart the pain can frequently be relieved. MacKenzie has pointed out that this is equivalent to blocking the nerve impulses of pain, which are referred from the spinal centers. The disturbed function of the heart itself is only manifest through the reflex spinal arc, because the nerves from the heart do not convey painful sensations. By blocking anywhere along

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

this arc, painful impressions are inhibited just as they would be blocked by a cocain injection. This definitely explains the mechanism by which counterirritants relieve pain in a deep organ, such as the heart, through treatment directed at a considerable distance from the diseased viscus. For quick results a mustard plaster is the best and handiest of these local pain-relieving agents. A few drops of chloroform in the palm of the physician's hand, then quickly applied and pressed over the painful region, and kept there despite the patient's protests, until there is a burning sensation felt between the physician's fingers, is a rapid and most efficient way of producing this counterirritation and consequent nerve-blocking. Any of the popular liniments will accomplish this result, but less effectively than the mustard. If the blocking is to be continued, the counterirritation must of course be kept up. In such cases, repeated applications of iodin or some other substance to produce blistering will usually be necessary. Sometimes a strapping of adhesive plaster keeps the chest quiet and so relieves the pain about the heart. This is the mechanism of the relief which sometimes follows the use of porous or belladonna plasters. For quick action, therefore, one can first use a counterirritant locally and Hoffman's anodyne internally. Turning the patient on his right side is occasionally successful.

Drugs.—For the distressing sensations about the heart, particularly the uncomfortable feeling about the apex, the smothering sensations, and the consciousness of a powerful extra-systole, cratægus has been found to be more satisfactory than any other agent for continuous use, although it often fails, as do all other remedies, which must be given blindly without any definite physiological indication. It is not a quickly acting remedy but must be given over long periods. In the author's experience it has been more successful in the aortic cases than in the mitral ones. The dosage is twenty minims (1.35 c.c.) t. i. d. of a good fluid extract or its equivalent. Much care should be exercised in securing an efficient preparation. It may be given for months at a time and does not have any deleterious effect upon the stomach. Its effect may often be enhanced by combining twenty grains (1.30 grams) of bromid with each dose.

Iodid.—For the relief of constant pains in the chest, especially those associated with aortic disease and referable to the sternum, the iodid of potassium is of unquestioned value. It is immaterial whether the cause is lues or arteriosclerosis. However, cases of rheumatic origin are less certainly relieved. As to just how the iodid accomplishes this is not known. Usually five grains (0.324 gram) of potassium iodid t. i. d. are sufficient. Organic iodids have been disappointing.

Severe Cardiac Pain and Distress.—When the pain is very severe, nothing short of morphin in full doses, grain 1/3 to grain 1/2 (gram 0.0216 to gram 0.0324), will suffice to give relief. This is especially true if there is an accompanying dyspnea. If there is no decided result from the first hypodermic of morphin in any cardiac case within half an hour, then, before giving another dose, one should warn the patient's friends that this is likely to be a serious attack. Patients who require more than 1/2 grain of morphin to relieve the pain are always in a dangerous condition and often die within a short time. The friends are often only too anxious to ascribe the fatal ending to the repeated use of the hypodermic medication. Of course, morphin does not kill by reason of any cardiac effect, and it should not be withheld, but the practitioner should always protect himself in such events by foretelling that death, should it occur, is due to the disease, and not the hypodermic medication. The

PRACTICE OF MEDICINE—TICE
☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

practitioner should not leave the patient if the pain is not relieved by these doses, as there is a strong likelihood that death is at hand.

Cramps in the Legs.—For the severe cramps in the legs so common in aortic disease which awaken so many patients in the middle of the night, the use of thick woolen stockings up to the knee, and long, snug-fitting woolen drawers, is often sufficient. The cause of this pain is probably analogous to the oppression and pain in the chest experienced by these patients on going out into the cold. About 3 a.m. the temperature of the room usually falls, and this may account for the appearance of the pain at that time. A hot water bottle in the bed is a good preventive. When it is not prevented by the warm stockings, placing the limbs in hot water during the attack may afford relief. In other cases it is necessary to administer tincture of opium, from 0.30 to 0.625 gram (5 to 10 minims) at bed-time each night, to prevent such attacks. The danger of contracting the opium habit is *nil* in the case of any cardiac patient who has reached this stage.

Buzzing and Noises in the Ear.—(Sensation of hearing the heart-beat in the ear, dizziness, etc.) All of these symptoms occur in cardiac patients, as well as in neurotics, but in almost all instances in the cardiac they are associated with some middle or internal ear lesion, which becomes noticeable to the patient only when compensation begins to fail. In taking the history it is necessary to find out just what the patient means by dizziness, etc., as generally his interpretation and that of the physician are different. Treatment devoted to the ear is of the first importance, and when a patient with cardiac disease complains of any of this group of symptoms, the ear must be considered as the primary cause until proven otherwise.

Bromids in twenty grain (1.30 gram) doses, three times a day, for this purpose, give more subjective relief than does any other medicinal agent.

Fainting Spells.—Fainting spells may occur in any form of valvular disease.

Aromatic spirits of ammonia internally, and smelling salts to the nose, and, most important, the recumbent position, are usually sufficient to bring relief.

Sometimes the patient uses the euphonious title "fainting spells" to denote true epileptic convulsions.

Pruritus.—For the pruritus so common in these patients one should first stop opiates and administer alkaline diuretics, excepting the bitartrates, which often seem to irritate the stomach; also the occasional use of diuretin; locally the lotion of calamine and zinc. If this is not successful, a preparation of carbolic as lotion or salve, in the proportion of five minims to the ounce, is indicated.

Bad Taste and Bad Breath.—These minor symptoms are seldom complained of unless the patient is asked specifically as to their presence. One or the other is quite commonly present during a break in compensation. Sometimes it is due to an empty stomach, i.e., when one passes regular meal time; in other instances from eating more than can be assimilated. Sometimes the sense of bad taste antedates the onset of other symptoms by a considerable period of time. There is nothing characteristic about this taste, but it is usually described as flat or bitter. Active catharsis by calomel, and diuresis obtained either by digitalis or diuretin in small doses, commonly gives relief. Many of these patients have a muddy complexion, which suggests the old-fashioned term biliousness. There is a coated tongue and loss of appetite. In such cases food containing eggs, butter, cream, milk, cheese, and fat should be rigidly eliminated from the diet, because no matter how the fact may be explained these foods do aggravate the symptom. The frequent use of small doses of calomel, supplemented by the daily administration of bile-salts, accomplishes a fair measure of success in this group of cases. Of course, one must inspect the tonsillary crypts as putrefaction here is sometimes responsible.

Parageusia.—The thick, slimy sensation in the mouth on awakening, as well as the dryness in the mouth, may be alleviated by rinsing the mouth with cold carbonic water—or by the use of chewing gum; sometimes spraying the nose at bedtime with a neutral oil accomplishes the same result. The salty, bitter taste, with parched feeling of the lips, is often intensified by taking saline cathartics. Vegetable cathartics are preferable in such patients.

Excessive Perspiration.—This is a common complaint in the stage of decompensation. It is sometimes nature's method of sparing the kidneys, and as such should be welcomed. At times it seems to bear a definite relation to the dyspnea. When the dyspnea is not urgent, the sweating is profuse, and **vice versa.** In the cases associated with diminished kidney excretion, diuretin often affords relief. In most cases atropin gives relief for a few days, but soon loses its effect. A vinegar sponge bath at bedtime is sometimes efficacious.

Hoarseness.—Hoarseness in anyone suffering from cardiac disease which does not quickly clear up should arouse one's suspicion that it is due to paralysis of the recurrent laryngeal nerve. When in doubt as to the etiology of the hoarseness, in the absence of means of making a laryngoscopic examination, one should instruct the patient to attempt whistling. If he does make the attempt, the cause of the failure is due to laryngitis, whereas the patient who is hoarse from nerve palsy will not even make the attempt. Treatment is of no avail, but nature herself does much to make the patient comfortable.

Broken Compensation

Sooner or later, in nearly all cases of valvular disease, the major symptoms are in evidence. Frequently the process is a gradual one, following the advent of the minor symptoms, or occurring because of an intercurrent infection which causes the muscle to give out quickly. This failure of the muscle can finally be predicted in any patient who has ever suffered from valvular disease, inasmuch as a lesion of either valve or muscle presupposes a coincident infection of the other. Once there is a break in compensation in general, the treatment must be the same, no matter what the particular lesion may be. Technically it is usually the treatment of tricuspid regurgitation—the final lesion in nearly all cases of broken compensation. Practically it consists in: (1) the treatment of the heart itself, (2) relieving congestion and disorders of physiology of other organs. Often the relief of these latter is more important than that of the heart, and once they are functioning normally the heart can take care of itself.

Rest.—Here again absolute rest is easily the most important of all remedial measures. There is now little trouble in securing the patient's consent to rest, but it is difficult to make him remain constantly in bed. One must enlist his coöperation; otherwise as soon as the physician leaves the house he will attempt to get out of bed. If the reason for his absolute rest is conveyed to him in language that is intelligible, obedience can usually be obtained.

In prescribing rest the physician must give positive and clear directions. Rest in bed must be absolute; if possible the patient is to remain on his back, or if dyspnea is marked, he may sit up in bed; he must use the bedpan and may not go to the table for meals. He should not be allowed to read the paper for the first three or four days, nor to see any visitors except his immediate family. A nurse should be employed at once, and she should be on duty at night during the first week of treatment, otherwise the patient will try to help himself when he needs attention. Of course any one who cannot use the bedpan should be allowed to use a commode in preference to catheterization, but cardiac patients usually learn to use the bedpan. Many patients cannot lie down because of dyspnea, and as a consequence they strenuously object to lying in bed unless they can have their feet on the floor. When this feeling of distress cannot be alleviated, the patient's wishes in this matter must be granted. Sometimes lying in a Morris chair solves the problem. Occasionally sleep can be obtained only while the patient is sitting up in a chair with his head bent forward on a pillow placed on a broad sheet supported on the arms of the chair. When this is the case this position must be allowed, but as far as possible the limbs should be kept in a horizontal position.

Diet.—The diet should be as dry as possible; certainly solids and liquids should not be partaken of at the same meal. If the patient is hungry one may usually allow dry toast, creamed potatoes, cereals, milk, malted milk, tea, coffee, ginger ale, chicken, or lamb chop, the total amount of fluid in twenty-four hours not to exceed 32 ounces (946 c.c.). As a rule the patient is not hungry, but is quite thirsty. Here again one secures his coöperation by explaining the necessity of restricting the amount of fluid intake so that it may be compared with the output, the urine being measured during each twenty-four hours. The urinary output is generally a good index of the progress of the case. Salt must be interdicted because it increases the thirst, and if there is any concomitant parenchymatous nephritis it increases the edema. Therefore, it is a good rule, in the presence of edema, always to restrict the use of salt in the food. In the absence of edema it is sufficient to take the salt-cellar from the tray or table. If the digestion is good, fruits may be allowed; otherwise, the restriction should be similar to those already described under the dietary management of the minor digestive disorders. Fats, butter, cheese, etc., should be eliminated.

Hope.—All cardiac patients suffering from any of the minor, and particularly any of the major, symptoms of decompensation should be given as much hope and encouragement as possible. No matter how bad the case may seem to be, immediate recovery is always possible, even though permanent recovery may be impossible. A positive reassurance must be given repeatedly, even though there is no question on the part of the patient as to how he is progressing. It is one of the best of medicines and yet is most begrudgingly given. It is surprising what a beneficial effect hopeful announcements have on the cardiac patient.

Digitalis.—A very large number of cases of broken compensation in valvular disease will react to absolute rest alone, if it is sufficiently prolonged and thoroughly carried out. We have in digitalis, however, a drug of specific value in some forms of cardiac disease and which is useful in the case of all patients suffering from decompensation, no matter what

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

the cause may be. In many cases of decompensation, no matter what the apparent contraindications to its use may be, every maneuver should be employed in an endeavor to give the patient the advantage of its use. When digitalis begins to act, there is an increase of the urine output, a lessening of dyspnea, and of the minor symptoms. If fibrillation is present, the weaker, ventricular contractions which do not reach the wrist are gradually eliminated and the pulse-beat approximates the apex-beat in frequency. The drug should be continued more or less throughout the life of the patient suffering from fibrillation.

ADMINISTRATION.—In general the effect of digitalis is to be measured by the amount of digitoxin contained in the preparation. The method of standardization depends upon the reaction of the heart of the frog or the cat to the drug. By the frog unit, which is the one in general use, is meant the amount of digitalis preparation, whether powder or liquid, *which* causes the arrest of the heart of a frog (of from 30 to 40 grams weight) in systole within thirty minutes. One gram (15.43 grains) of an ordinary good preparation of digitalis in powder form equals 50 frog units; therefore, 0.1 gram (grains 1.543) of such a powder equals 5 frog units. In general 20 frog units in a day is a fair dose. Of late the cat unit has been substituted by many pharmacologists. In any event the equivalent in cat or frog units of each preparation, whether it is a new proprietary or an old galenical, should be known before it is accepted for use.

The method of Eggleston, otherwise known as the body-weight method, is growing in popularity. This is especially true in hospital practice. It is founded on the principle of full digitalization within from ten to twenty hours after the beginning of the administration of the drug. The total amount is expressed in terms of the activity of the drug and of the patient's body weight in pounds. The cat unit is the standard employed. This is the quantity of the dry drug in milligrams which is required to kill one kilogram of cat when given slowly and continuously by the intravenous method (Hatcher). The average requirement for a man is 9.15 cat units for each pound of body weight. A cat unit is equivalent to 100 mgs. (1.54 grains) of an ordinary good tincture. For an ordinary patient weighing 150 pounds, about 20 c.c. (5.42 fluidrams) of a good tincture is necessary. For accuracy any one of the following formulæ of Eggleston may be employed:

$$\text{Formula I: } \frac{\text{C. U.} \times 0.15 \times \text{W}}{1{,}000} = \text{Grams of powdered leaf in total amount.}$$

$$\text{Formula II: } \frac{\text{C. U.} \times 0.15 \times \text{W}}{100} = \text{Cubic centimeters of tincture in total amount.}$$

$$\text{Formula III: } \frac{\text{C. U.}}{100 \times \text{W}} = \text{Cubic centimeters of infusion in total amount.}$$

In these formulæ, C. U. is the number of milligrams in one cat unit, and W is the patient's body weight in pounds. The following example illustrates the use of these formulæ: A patient weighs 150 pounds, and the digitalis available has an activity of 100 mg. to the cat unit. Applying Formula I for the powdered leaf, we have 100 × 0.15 = 15; 15 × 150 = 2,250; 2,250 ÷ 1,000 = 2.25 grams of leaf in total amount. Applying Formula II for the tincture, we have 100 × 0.15 = 15; 15 × 150 = 2,250; 2,250 ÷ 100 = 22.5 c.c. of tincture in the total amount. Formula III gives 100 ÷ 100 = 1; 1 × 150 = 150 c.c. of the infusion in the total amount.

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.
PRACTICE OF MEDICINE—TICE

ADMINISTRATION OF AVERAGE CALCULATED TOTAL AMOUNT.—When the patient has received no digitalis within the preceding ten days, and the case is urgent, from one-third to one-half of the total calculated amount is administered at the first dose. After an interval of six hours, from one-fifth to one-quarter of the total is administered. After a second six hours, from one-eighth to one-sixth of the total amount is administered. Thereafter, if more digitalis is needed, about one-tenth of the total amount may be repeated every six hours until maximal digitalization is secured. In the case of the example given above with the total amount being 22.5 c.c. (6.09 fluidrams) of tincture, the first dose would be from 7 to 11 c.c. (1.89 to 2.98 fluidrams), the second from 4 to 5 c.c. (1.08 to 1.35 fluidrams), the third from 2.5 to 3.5 c.c. (33.2 to 49.0 minims) and thereafter about 2 c.c. (32.4 minims) every six hours if required.

When digitalis is given by this method, its effects begin to become evident on the electrocardiogram within four hours and reach the maximum within another four hours and continue thus for twenty-four hours. The rate of excretion of digitalis following such dosage amounts to approximately 20 minims (1.25 c.c.) per day so that the effect of this dosage lasts for four or five days; after this it is necessary to give from 20 to 30 minims (1.25 to 1.90 c.c.) twice daily. When the method is used in private practice, the patient should be carefully observed for the first two days at least; it is indicated in severe attacks of decompensation especially if there is any objection to the use of opium. However, the average physician does *not* feel that it is *safe* to use these large doses in *private* practice; furthermore, the necessity for rapid digitalization is rarely necessary in private practice. Ordinarily 20 minims (1.25 c.c.) of the tincture four times a day is a sufficient dose. The best preparations, containing the largest amount of digitoxin, are those obtained from the English leaves. Allen's English leaves have a world-wide reputation. The powdered leaf is quite the most efficient of the digitalis preparations. If the irritating effect on the stomach produces nausea, it may be given in capsules. Furthermore, many patients have digestive disturbances from alcoholic solutions of medicines of any kind. However, most practitioners prefer to use the tincture. In passing, it may be mentioned that one should specify the druggist who is to fill the digitalis prescription, or the pharmaceutical firm that manufactures it, because the average drugstore tincture of digitalis varies as much as 50 per cent. in strength. The tincture may be conveniently prescribed in combination with elixir adjuvans as follows:

℞ Tincturæ digitalis....................fʒvi (22.50 c.c.)
Elixir. adjuvantis q.s. ad..............f℥ij (59.20 c.c.)
Sig. fʒj (3.75 c.c.) t.i.d. p.c.

This obviates the necessity of accurate measurement of the dosage at each administration. It insures accuracy and obviates some of the disagreeable taste and odor of the drug.

A common error is to consider that minim equals drops. This is a frequent cause of the failure to achieve results. For instance, from 18 to 30 drops represent 10 minims of the tincture of digitalis. This variation is due to (1) the shape of the dropper, (2) the position in which it is held, (3) the speed at which it drops, temperature, etc. For this reason it should be prescribed rather with some excipient, making so many minims to the large teaspoonful.

Any other menstruum which does not precipitate the digitalis may be used. The powder may be given in wafer or in capsule form. When digitalis is administered over long periods of time, a dose of calomel or blue mass given once a week adds to its efficiency. The infusion of digitalis has a widespread reputation, in that it is of particularly great value in the cardiac dropsies. Some of this good effect is due, doubtless, to the relatively large doses of digitoxin which the patients receive in the usual dose (½ oz. [15 c.c.]) rather than to the former belief that the digitoxin keeps in suspension some of the active principles not largely contained in the tincture.

The fluid extract of digitalis in tablet form is a convenient way of treating the minor symptoms of ambulant cardiac patients, but it is not nearly so reliable as the other preparations. It may be given in tablets containing 2 minims (gram 0.12) three times a day. In producing digitalization by any method, one should give the drug until physiological effects are obtained. These physiological effects are nausea, vomiting, diarrhea, extrasystoles not previously present, and the presence in the pulse of coupled beats. A very long interval between the second and first beats is characteristic of digitalis toxemia. One listens, and the interval seems so long that doubt arises whether the following first sound will ever appear.

Loss of appetite is the earliest sign of intolerance. It may not be accompanied by vomiting, and it may not last more than a few hours.

When any or all of these phenomena occur, the drug should be discontinued for a few days, and then begun again at one-half the former dose. It must be kept in mind that the effect of digitalis on the stomach is a twofold one. On the one hand, there is the early local, irritating effect, as well as the nauseating taste, and these account for some of the gastric symptoms. On the other hand, the central effect is a later phenomenon and signifies a saturation for that individual. This later phenomenon will occur with any preparation of digitalis which exerts a sufficient physiologic effect to make its use worth while. There is no known way to obviate these central symptoms when the full physiologic action has been obtained. However, some preparations do not have the same local effect on the stomach that others do, and consequently have a wider range of usefulness.

Other Preparations of Digitalis.—The French granules of Nativelle are made up largely of digitoxin; they are an efficient preparation and are always reliable. When the stomach will not bear medicines of any kind, it is better to resort to hypodermic medication. For this purpose the digitalin so much used in the past is generally inefficient. If it is used, it should be given in large doses, grain 1/50 (gram 0.00132). The newer preparations, such as digalen, digipuratum and digifolin, are much more elegant and efficacious. It is sometimes possible to administer digitalis in the form of an alkaline solution of digipuratum by rectum, but it is unreliable. Within the last few years, a number of new preparations of digitalis have come into use.

Digalen.—Of these preparations just referred to, the most commonly used is digalen, said to be a solution of digitoxin, but believed by other pharmacologists to consist largely of digitalein. It is unquestionable that this does not disturb digestion to the same extent as the tincture, but the author does not feel that he has often witnessed decided beneficial results from its administration by mouth, even when large doses were employed. It is, however, a convenient form for hypodermic use. It has been stated that it is more than ten times as expensive, unit for unit, as the tincture. There is no question but that the physiological results follow its use when given intravenously, and in emergencies it is the form most generally applicable. The dose in any case should be at least 20 minims (1.25 c.c.).

Digitan.—This is a preparation of the leaves from which much of the irritative material, including digitonin, which locally irritates the stomach, has been removed. Of course, the action of the digitalis on the digestive tract remains so that digestive symptoms following its administration are not entirely lacking. It is obtainable in two forms, the tablets containing 0.1 gram (grains 1.543) and a liquid containing 1 c.c. digitalis leaves, or 8 frog units. Usually 12 tablets are necessary to produce an efficient digitalis effect; one tablet four or five times daily is the usual dose. Hypodermically, the dose is the same as by the mouth. When given intravenously, for an emergency, one dose of 2 c.c. (32.4 minims) is usually sufficient. Similar preparations on the market under the name of digifolin and digipoten are now in general use. The results are similar to those of the digipuratum.

Substitutes for Digitalis.—Nearly always when digitalis fails the substitute also fails, but one must, figuratively speaking, follow the example of the drowning man, and grasp even at a straw. Of these straws strophanthus is the one most commonly employed. Theoretically, it is an ideal preparation. In practice it usually fails. The fact that it has no unpleasant taste often leads physicians to prescribe it in place of digitalis. If the true physiologic digitalis effect is obtained, the central effects are just as irritating as are those of any of the digitalis-like bodies. The dosage which produces physiologic effects, and the poisonous dose, are so close that it is much feared by laboratory workers. Generally five minims (0.3 c.c.) of the tincture three times a day is a sufficiently high dosage. Strophanthin is given intravenously. Crystalline Strophanthin derived from Strophanthus gratus is known as Oubain. Oubain is twice as strong as Strophanthin Kombe. This difference in dosage is usually neglected in the various treatises on this subject. Strophanthin thus may be substituted for digitalis. It is usually administered by intravenous injection. Great care must be exercised in giving intravenous injections, because perivascular infiltration of even the smallest quantities causes a very severe local reaction.

It is obtainable in ampoules containing one milligram (1/64 grain) of the Amorphous Strophanthin and of Oubain in gr. 1/125, the equivalent of 15 frog units. The effect is very prompt. Because of its toxicity, the drug should be reserved for acute attacks of decompensation, when there is immediate danger to life. It should not be repeated nor used if much digitalis has recently been administered, nor should a large dose be repeated within twenty-four hours. Occasionally death follows its use, but it is generally difficult to determine whether the patient would not have died anyway.

Indications for the Use of Digitalis.—Digitalis is, of course, specific only for those who suffer from auricular fibrillation, because of its effect in blocking the impulses which pass through the bundle of His. However, it is of inestimable value in other diseased conditions of the heart, and particularly in right heart failures. It is more effective in heart failure due to rheumatic fever than when it is due to other causes. As to its use in aortic regurgitation, theoretically, it should not be used in the compensated cases, and practically it is not well borne in these cases, except in small doses, unless the aortic regurgitation is due to rheumatic endocarditis. However, when a right heart failure is associated with the aortic regurgitation, as evidenced by dropsy, etc., digitalis should be given with just as free a hand as in any other form of right heart failure; except in the presence of these symptoms, it is not well borne. In some cases of primary mitral stenosis in which symptoms are present and yet there is no enlargement of the heart, the drug is not well borne. In regular hearts the result is not so gratifying as it is in fibrillating hearts. Under its use in these cases, the heart-beat is slightly slower, diastole is lengthened, and the contraction of the ventricle is strengthened.

Contrary to what was formerly believed, the drug is frequently indicated in the decompensation of many patients suffering from high blood-pressure. This is especially true if there are evidences of stasis or any other signs of cardiac failure. In any such case, no matter what the apparent physiological contraindications may be, digitalis should be tried. Many patients who appear to be ideal subjects for the use of a nitrite react to digitalis and to nothing else. It is also indicated in cardiac insufficiency associated with a renal involvement. It is entirely useless in many of the functional disturbances, such as palpitation, extrasystole, tachycardia, etc. In fact it commonly makes these patients feel worse. Finally, there should be no hesitancy in the use of this drug in moderate dosage in any case of decompensated organic heart disease at any time, provided there are no digestive disturbances. It is a drug the efficiency of which does not wear off. It is just as efficient after long use as after short use; its effect on the heart, all other things being equal, is the same one year as another. It should be given in small doses in the early minor disturbances of the cardiac patient. Often it renders possible the use of other remedies employed for the relief of these minor symptoms, when without its use nothing could be accomplished; this is especially true in the treatment of the winter bronchial attacks of cardiac patients whose hearts are apparently compensating.

Contraindications to the Use of Digitalis.—Indications to cease the use of digitalis are: (1) those referable to the heart and circulation; and (2) those referable to its effects on other organs. Among those referable to the heart itself are: (*a*) a marked grade of sinus arrhythmia that is independent of the respiration and is phasic in type; (*b*) premature contractions when not previously present, especially in the form of pulsus bigeminus, the " coupling of beats at the wrist " as discussed by the older writers (this is particularly noticeable on sitting up in bed); (*c*) ventricular tachycardia; (*d*) partial or complete heartblock, and (*e*) true nodal rhythm—a very long pause between the second and first sound of the heart that gives one the impression that the heart may not beat again—is sometimes an evidence of digitalis toxemia. Fortunately these signs can, in almost every instance, be determined clinically without the use of instrumental means. As to the second group, i.e., its effects on other organs, the symptoms of such effects are most insistent and are Nature's own efforts for safety. They are nausea, vomiting and diarrhea. When such symptoms follow the first few doses of the drug, they are almost always the result of a local irritation of the stomach itself, and should not constitute a contraindication to the use of the drug, but rather to the way of administering it. However, when they occur after some days of its use, or after the administration of large doses, they call for its prompt discontinuance. The suggestion that extreme hunger and hunger pangs are among the earliest evidences of digitalis toxemia has been

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

PRACTICE OF MEDICINE—TICE

made by Neuhof, and the author has often confirmed this finding. These symptoms may precede the major symptoms by a day or two. If an intercurrent disease is present, which is associated with fever, the dosage of digitalis should be greatly increased because of the clinical observation that its effects are decidedly lessened in the presence of temperature. Of course, no one should give the drug for the treatment of acute endocarditis as such, nor in the hope that it will control a rapid action of the heart from any cause, except where there is an old lesion present, preceding the acute exacerbation. It is usually only when such a lesion is rheumatic in origin that such control will be evident. The use of the drug for the purpose of slowing the heart is in acute diseases perhaps the commonest therapeutic error in medicine.

Time of Administration.—No matter what preparation is employed, it is best to give it after meals, rather than on an empty stomach. It is seldom necessary to administer it more than four times a day. When once the physiological effect is produced, it continues, and two doses each day are sufficient.

Quinidine.—A new departure in the treatment of heart disease has been established by the introduction of quinidine. This is neither a stimulant nor a cardiac tonic, but it has the peculiar ability of sometimes being able to abolish auricular fibrillation, so that a heart that has been acting irregularly will beat regularly. It is efficient in doing this in a varying proportion of cases. It is usually successful (1) in the cases of paroxysmal fibrillation, (2) in about one-half of the early cases of well-established fibrillation, (3) in a few of the confirmed cases. Frequently these relapse. Pardee considers it efficient in about forty per cent. of the cases, and this represents the most favorable view of the matter. The normal rhythm persists for a longer or shorter period, but usually when the drug is stopped the irregularity returns. In advanced disease of the heart, with enlargement, it is not often that recovery takes place. Generally speaking no one can foretell which patient will or will not be affected by quinidine, so that it is safe practice to try out quinidine in every case just as soon as the danger of decompensation is past. At the present it is not wise to use it in acute attacks of decompensation. Among the dangers following its use are (1) its depressant action in cardiac contractibility, (2) its tendency to produce a very rapid pulse and rapid ventricular rate. This induces fatigue of the heart, and must be counted against quinidine; (3) its tendency to produce sudden death. In these cases it is believed that death is due to cerebral embolism from clots arising from the interior of the left auricle. It is unwise ever to administer it except when the patient is under close and continuous observation, either in home or in hospital.

Because of its occasional ill-effects one should begin with 3 grains three times a day, slowly increasing to 6 grains t. i. d. If there are no results in five days it may be stopped. The usual sequence in the fortunate cases is for the heart to change from fibrillation to auricular flutter, and then to normal rhythm. In a few patients after the attainment of normal rhythm this rhythm has continued for months, and even years thereafter. Generally speaking, the longer the fibrillation has lasted the more refractory the heart is to quinidine. The cause of the cardiac lesion does not seem to affect the prognosis as to its successful results.

Opium.—Next to rest and digitalis, opium is the most necessary agent in the treatment of heat failure associated with chronic valvular disease. It is absolutely necessary to relieve the severe pain that frequently accompanies this disease, and should then be given in the form of a hypodermic of morphin. For the distressing dyspnea it has no equal in our armamentarium. For sleeplessness it is the only agent which can always be relied upon. It produces a more constant lowering of blood-pressure than any other medicine. It does not cause as great a fall as the nitrites do, but produces a more lasting effect. This it does through its calmative effect upon the nervous system. The nervous element in most cardiac patients is responsible for an increase of from 10 to 30 mm. Hg in blood-pressure and this is overcome by small doses of the narcotic. There are very few contraindications to its temporary use in cardiac disease. Of course, digestive disturbances following its use are not uncommon, but they are not any more marked than they are in patients suffering from other diseases; indeed, one often feels that they are less so. The drug is contraindicated in acute gastric dilatation as pointed out elsewhere. It is not absolutely contraindicated in renal disease if the kidneys are moderately active. While it is not excreted through the kidney, yet in case of any patient suffering from a very marked diminution in urine, unless other indications are absolute, it should be employed with caution. It is difficult to say whether such patients go into coma because of the kidney disease or because of the effect of the narcotic, but it is better practice to withhold it unless the distress is very great.

Pantopon.—Pantopon has been introduced to offset some of the disagreeable side effects of opium.

Pantopon is a reddish-brown soluble powder; it contains the active principle of opium, and is devoid of its extractives. It is absorbed more quickly, does not produce nausea, is less depressant on the respiratory centre than is morphin. It does not produce as much intestinal stasis as opium. It is marketed in tablets of gr. 1/6 or in ampoules representing gr. 1/6. It is administered by mouth or by hypodermic injection.

Administration.—When the symptoms are not decidedly urgent, the use of the deodorized tincture in doses of 7½ minims (0.5 c.c.) every four hours is commonly sufficient. This may well constitute the first prescription in any case whenever the patient has not slept for several days or is suffering distress. Sometimes codein may be substituted for the opium with fewer disagreeable effects upon the digestive tract. Codein is especially valuable in the coughs of the cardiac patient. In the presence of severe symptoms morphin from grain one-third (gram 0.0216) to grain one-half (gram 0.0324) hypodermically is commonly necessary. When the drug itself is given by mouth, it is best to combine it with a pleasant menstruum, as the taste and odor are disagreeable to some patients. Either the elixir adjuvans or the aromatic fluid extract of cascara sagrada are useful for the purpose. Of course its use should not be continued any longer than is necessary to relieve the urgent symptoms, but on the other hand it should never be withheld because of the fear that the patient may contract the habit, or because of any mawkish sentimentality as to " doping." It is almost an unheard-of thing in a large hospital service to meet with a patient who has contracted the habit from the employment of the drug for the relief of the symptoms of true cardiac disease. The cardiac patient who requires the constant use of a narcotic for a long time is likely to die in any event, and it is cruelty not to afford relief when it can be obtained. At the present time, there is, on the part of the younger practitioners, a disinclination to use the " dope " as it is called, or any other agent which only relieves the symp-

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

toms of disease rather than the cause of the disease itself. The attainment of any such object as a cure in the treatment of cardiac disease is only an evanescent dream. In the present state of our knowledge the treatment of symptoms must constitute at least 90 per cent. of our therapy, and opium is easily the king of all agents which may be used in relieving the symptoms of cardiac disease. It is always difficult to impress sufficiently upon the mind of the student that opium does not kill through its action on the heart, but rather through action on the respiration, and that it is not a heart depressant.

Caffein.—Caffein itself is of a limited use as a diuretic, except as a temporary stimulant; it is of little value as far as the heart itself is concerned. In the form of **diuretin,** grains 10 to grains 20 (gram 0.65 to gram 1.3), four times a day, or **theocin,** grains 2 to grains 5 (gram 0.13 to 0.324), it is an efficient diuretic, particularly of service where there is coincident disease of the kidney. If digitalis of unquestioned efficiency is employed in sufficiently large doses for a week, with no effect on dropsy, then diuretin should be substituted for three or four days. Frequently such an alternation is useful throughout the whole course of treatment.

Nitrites.—Nitroglycerin is of value as a means of relieving acute symptoms, rather than for the production of any permanent effect.

Frequently the administration of the drug at regular intervals will prevent the occurrence of painful attacks. In other instances it is best given just before the patient goes out for a walk or immediately after meals before any exertion.

It is in the relief of paroxysms of anginal pain and dyspnea consequent on cardiac disease that its most striking effects are observed. The effect of a tablet of nitroglycerin (grain 1/100 [0.00065 gram]), when allowed to dissolve under the tongue (and this is the best way of administration), is apparent in less than three minutes, and continues for half an hour, but the symptom for which it is given often does not return for days thereafter. The patient should be warned of the sense of fullness in the head that so generally follows its use. The peculiar sensation makes nervous patients apprehensive. The hypodermic tablets are generally more reliable than the tablet triturates. The action of nitrite of amyl is generally unsatisfactory.

Strychnin.—The effect of strychnin is really exerted upon the spinal nervous system, and it does not have any appreciable effect upon the unstriped muscle of the heart. It does stimulate the general muscular system, and increases the depth of respiration. It does not (as has been so generally stated in the text-books of the last decade) act as a tonic on the heart. Its effects have no possible resemblance to the action of digitalis. If the symptoms of neurasthenia are present, it commonly makes the patient feel worse.

Atropin.—The author has not found belladonna, or atropin, to be of any decided service in relieving minor symptoms. To alleviate the nocturnal attacks of dyspnea which prevent the patient from sleeping, the use of a full dose, grain 1/100 to grain 1/75 (gram 0.00065 to gram 0.00086), given late in the evening hypodermically will sometimes ensure regular breathing throughout the night. The author has never been able to convince himself of the efficacy of the belladonna plaster in relieving cardiac pain. It is of use at times in overcoming pulmonary edema.

Bromids.—For the relief of many of the minor symptoms bromid does what opium will do for the alleviation of the major symptoms. It frequently satisfactorily relieves palpitation, quiets nervous apprehension, and thus soothes the tumultuous action of the heart. It is of especial service in the aortic cases. By quieting the nervous system it materially lowers blood-pressure. With the exception of opium its effect in this respect is more *lasting than when pressure is lowered by any other agent. It is well to continue its use on and off, alternating with potassium iodid* and with cratægus. *It must be given in full doses,* 20 to 30 grains (1.30 or 1.95 grams) two or three times daily. Less than 20 grains (1.30 grams) at a dose is absolutely useless. One cannot too often repeat that the dosage of all drugs in cardiac disease must be high as compared with their use in other conditions. Mistaken dosage accounts for far more failures in cardiac therapy than mistaken indications. When there is bromid intolerance or severe acne from its use, **valerian** does to some extent take its place, pharmacologists to the contrary, notwithstanding. **Allonal** in 2½ grain doses is frequently a good substitute.

Calomel and Mercury.—The indication for the use of the mercurials is clear enough in luetic cases, but their occasional service in other cases is not so clear; yet the clinical evidence of their value is unquestioned. Frequently in an undoubted rheumatic mitral lesion, with steady progression, and in which nothing seems to stop the increasing dropsy and dyspnea, the use of calomel, either as a single dose, or given three times a day, will produce a marvelous result. It is believed that much of this is due to the diuretic effect of the mercury. Therefore, it is a good rule in any case that has not reacted to ordinary medication to prescribe a Niemeyer pill containing calomel, squills, and digitalis, $\bar{a}\bar{a}$ grain 1 (0.065 gram) t. i. d. for three days.

The drug must not be given for more than three days at a time because of the danger of salivation. Sometimes blue mass may be substituted for the calomel.

Aconite.—The field of usefulness of aconite in valvular disease is a very limited one. Occasionally in aortic disease with a very much perturbed heart, cyanosis, cardiac pain and oppression, the use of a few doses of the tincture of aconite affords relief when nitrites fail. The physiologic effect of the drug is only produced in such cases by the use of enormous doses. It appalls most practitioners to be told that the dosage should be between 20 and 30 minims (1.25 and 1.895 grams) repeated every three hours. The writer has not found its continued use successful in controlling symptoms. Such large doses do not produce the toxic effects which commonly result in normal individuals from the ingestion of a similar dosage.

Oxygen.—Oxygen is occasionally of service in the cyanosis of decompensation. One can never tell definitely in which cases it will be beneficial. It is given better by ether mask or by tube with Y attachment, through nares; here it increases oxygen in the blood. At times oxygen does give decided relief. It is given for from ten to twenty minutes every two hours.

Spartein.—Spartein is rarely of service, and may be given during an interval when the digestive tract is rebellious to the digitalis bodies. It sometimes produces prompt diuresis. The dosage is grain ½ (0.0324 gram) or more every four hours.

Adonis Vernalis.—This drug has not been successful in the author's experience.

Apocynum.—This is the vegetable trocar of the eclectics, and has a well-deserved reputation in patients who, figuratively speaking, are unaware of the fact that they have a stomach. The local action of the drug on the stomach is often irritating, and the drug must frequently be discontinued. The physiological action is due to the digitalis-like bodies. Where it does act well, the results are truly marvelous. The dropsy disappears as if by magic. It is well nigh impossible to prophesy when it will be efficacious, but it is always one more straw to grasp at when other agents fail. The Boston school deny that either apocynum or squills have any value, but clinical experience refutes this assertion. The dosage is 10 minims (0.6 gram) every four hours. An active principle has been on the market, but has not been satisfactory.

Squills.—Squills contains the digitalis-like bodies, and would be ideal were it not for the local irritating effect on the stomach. In the mercury pill its synergist action is of great service. The dosage is from one to five grains (gram 0.065 to gram 0.324) of the powdered drug.

Novasurol.—Within the last few years a new preparation known as novasurol has come into use for the purpose of inducing diuresis in the cardiacs. It is a double salt of oxymercuri-chlorphenoxyl, sodium acetate and diethylmalonylurate and contains 33 per cent. mercury. It is soluble, and may be administered intramuscularly and intravenously. It is only in edematous patients that it is successful. It aids markedly in the excretion of sodium chlorid and of water. At times its results are marvelous; more often it fails. It may produce a magical result in edema of the serous cavities. Its action becomes evident within twenty-four hours after injection. The contra-indications to its use are acute glomerulonephritis and enteritis; occasionally it produces severe stomatitis and gingivitis and an annoying colic and diarrhea. It was originally introduced for the purpose of treating syphilitic cardiacs with edema, and in such it finds its greatest field of usefulness, but is often of service in other cardiac edemas. The dose is one ampoule (1 c.c.) given daily for two or three days. In less severe cases the injection may be given every two or three days for three doses.

Therapeutic Measures Other Than Drugs.—Nauheim Bath.—Before the war the Nauheim baths had acquired, especially among the laity, a widespread vogue. Because of the special physical effect perceived by the patients themselves, as well as because of blood-pressure changes recorded by enthusiastic Spa physicians, the hope was planted in the patient's minds that not only could relief of symptoms be had, but that actual cure was to be attained by the baths. There is no question but that well-defined physiologic effects occur following these baths. The skin is reddened and blood-pressure raised or lowered, depending upon the temperature of the bath.

The Nauheim bath consists in immersion in a saline bath, containing a large amount of carbon dioxid. The physiologic effects depend (1) upon the temperature of the water, and (2) upon the contents of the water. The effect of a cold bath is well known—a lowering of the pulse-rate and increase of blood-pressure—whereas a hot bath causes an increase in pulse frequency. In the Nauheim bath, in addition to the temperature, the effect depends upon the carbon dioxid liberated. There is no direct effect on the heart itself from the use of the bath; its gain is an indirect one. The dilatation of the superficial capillary circulation as well as the deep vessels increases their capacity and thus takes the burden off of the heart for the time being. The dilatation of the vessels of the skin is simply due to the carbon dioxid contained in the bath; the salts also have a similar effect but to a less degree. This produces a

PRACTICE OF MEDICINE—TICE

☛ **Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.**

sensation of tingling and warmth over the whole body, thus making the bath seem much warmer than it really is. Within five minutes, there is a perceptible diminution in the respiration and the pulse is definitely slower within ten minutes. The composition of the bath consists of carbon dioxid, calcium chlorid and sodium chlorid. In the baths at Nauheim, the carbon dioxid is contained in the spring water. The ordinary method employed at Nauheim is as follows: A hot bath lasting from five to ten minutes is given at a temperature of 95° F. (35° C.); after this the temperature is reduced one degree Fahrenheit each day until 86° F. (30° C.) is reached. At the same time, the bath is prolonged one minute longer each day and the amount of salt is gradually increased. After the bath, the patient should be placed in a recumbent position and lightly covered; he must remain quiet for an hour or two, care being exercised that perspiration does not occur. A full course consists of twenty baths, followed by a period of rest of a month or so, to be followed by a second course. The same physiological effects may be obtained from the artificial Nauheim baths administered in the home. Many of the large commercial drug houses put the salts and acid in convenient form for the ready making of the Nauheim baths.

The Nauheim Bath at Home.—In the home it is advisable to begin with the so-called salt bath. The carbonated effervescing baths should never be employed at the first treatment. The first bath contains 5 pounds of salt and 6 ounces of calcium chlorid in 45 gallons of water. The quantity of salt and calcium is added, 1 pound of the former and 1 ounce of the latter until 10 pounds of salt and 11 ounces of calcium chlorid are employed. At the tenth bath, the carbon dioxid is introduced. The first effervescent bath consists of: 50 gallons of water at a temperature of 90° F. (32.22° C.) and 5 pounds of sodium chlorid, 1 pound of calcium chlorid, 8 ounces of sodium bicarbonate and 225 c.c. HCl. The first three ingredients are mixed in the water and then the acid is slowly added and stirred; the amount of sodium bicarbonate and acid are gradually increased day by day thus producing an increased elimination of carbon dioxid. At first, the duration of immersion is from three to four minutes. This is increased from one to two minutes at each succeeding bath. The first bath is given at a temperature of 96° F. (35.6° C.). This temperature is lowered by 1° F. (0.55° C.) every second bath, down to 93° F. (33.9° C.). After the bath, the patient goes to bed for at least an hour; a hot water bottle is put in the bed; chilliness means that there should be an increase in temperature of the bath. The baths may conveniently be given for two days in succession and, if circumstances permit, on the third day exercises may be employed. From twenty to thirty baths constitute a course. As a complementary measure, exercises are usually given in connection with the baths at Nauheim. These exercises were originally advocated by Schott and may be varied. Any of the ordinary anticonstipation exercises, not done too actively, will answer, the chief point being that the patient should not be tired as a result of the work.

Exercise.—When compensation has not been seriously disturbed the exercise of the patient's daily avocation is sufficient. When, however, there has been an attack of decompensation, even during convalescence, recovery is often materially hastened and the patient's own condition improved by careful exercise. At first, these exercises should be administered by the physician himself, or by a competent assistant. In the beginning they should consist of ordinary resistance motions.

Unless the exercise prescribed is pleasurable to the patient, it will seldom be continued and unless some one else goes through it with him at the time, he will soon tire of it. In the offices of those devoting themselves to cardiac disorders, it is customary to have the nurse accompany the patient through such exercises at regular intervals. The following are the exercises as recommended by Schott himself in the Brunton lectures:

1. The arms are to be raised slowly outward from the side until they are on a level with the shoulders. After a pause they should be slowly lowered.
2. The body should be inclined sideways as much as possible toward the right and then toward the left.
3. One leg should be extended as far as possible sideways from the body, the patient steadying himself by holding on to a chair. The leg is then dropped back. The same movements are repeated by the other leg.
4. The arms are raised in front of the body to a level with the shoulders and then put down.
5. The hands are rested on the hips, and the body is bent forward as far as possible, and then raised to the upright position.
6. One leg is raised with the knee straight forward as far as possible, then brought back. This movement is repeated with the other leg.
7. With the hands on the hips, the body is twisted round as far as possible to the right, and then again to the left.
8. With the hands resting on a chair and the back stiff and straight, each leg is raised as far as possible backward, first one, then the other.
9. With the fists supinated, the arms are extended outward, then inward at the level of the shoulders.
10. Each knee is first raised as far as possible to the body, then the legs extended.
11. This movement is the same as 9, but with the fists pronated.
12. Each leg is bent backward from the knee and then straightened.
13. Each forearm is bent and straightened from the elbow.
14. The arms are brought from the sides forward and upward, then downward and back as far as they will go, the elbows and the hands being straight.
15. The arms are put at a level with the shoulders and then bent from the elbows inward and again extended.
16. With the arms in front at a level of the shoulders and the hands stretched, the arms are opened out sideways and then brought together.
17. The arms are bent from the elbows, lifted outward and extended. The essential part of the movement is that the movement be slow and regular.

Practically few patients who are able to be about can afford the time or money for such luxury. Instead of this, walking on the level is a form of exercise within the reach of all and is quite as efficient. Common sense will teach how many blocks the patient can walk without fatigue and the number can gradually be increased. The value of Nauheim baths as a therapeutic measure is a somewhat debatable one. This much may be said,—they are of value only in the treatment of the patient who is suffering from the minor symptoms of decompensation, provided that he feels better after their use. Certainly they are not indicated in the presence of any of the major symptoms of decompensation. The effect of the Spa surroundings is often of more value than the baths themselves. They serve to bring the patient under medical supervision from time to time, which is of greater possible value to the patient than the reaction to the bath. Human nature demands that something physical be done, aside from the mere rehearsal of symptoms and advice and these baths are of service, just as electricity, high frequency, or any other similar physical measure would be. However, psychophysic methods to be followed in a religious manner such as the Schott and Oertel methods have never become popular in this country.

The aim of these various systems is to increase the compensatory reserve of the heart muscles of the body, in a pleasant and agreeable way, with little discomfort to the patient. It is only applicable to a

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

PRACTICE OF MEDICINE—TICE

limited number of obese and wealthy patients, and is best carried out in an institution devoted to this work.

THORACENTESIS.—Patients suffering from severe decompensation should be examined daily for indications of fluid in the serous cavities. It is particularly apt to occur insidiously in the pleural cavity. The right side is more often affected than the left. This may be ascribed (1) to the fact that most cardiac patients lie on the right side, and (2) to the obstruction of the mouth of the major azygos veins from the pressure of the dilated right heart.

Thoracentesis should be done whenever breathing is markedly interfered with, in the presence of a demonstrable effusion. Left-sided effusions must be especially watched, and whenever the effusion extends above the lower angle of the scapula, it should be drawn off. On whichever side it may be, when it is up to the fourth rib, the chest should be aspirated. If there is any fear of collapse, a small amount of novocain may be injected at the site of puncture, five minutes previous to the aspiration. Sometimes the operation is best done with the patient in the recumbent position.

PARACENTESIS ABDOMINIS.—Paracentesis should not be lightly undertaken until all other methods of relief of the ascites have been tried because it often disappears. Sometimes ascites develops before there is a marked general edema. In such cases there is often a preexisting cirrhosis of the liver. This would not of itself produce stasis in the abdominal cavity, but the added congestion due to the weakness of the heart is sufficient to obstruct the portal vessels and produce the ascites. The ascites should be aspirated whenever it is sufficient to interfere with respiration. Unfortunately it frequently soon returns.

In the presence of well-marked edema of the legs which does not react within four days to digitalis, the insertion of two aspirating needles in each limb, and occasionally a small one in the scrotum, is followed by a profuse loss of fluid, often amounting to a couple of quarts. Southey's tubes are seldom in the possession of the practitioner, and the aspirating, or large caliber hypodermic needles, are just as efficient. Ordinary care is necessary to prevent infection. The skin should be treated just as carefully as prior to an ordinary operation. After the puncture the needle and leg should be surrounded with sterile gauze. The excreted fluid is irritating, and if the discharge continues for more than a few days it produces eczema, causing the practitioner to fear that the wound is infected. This is rarely the case, and if a weak carbolized or boric-acid compress is applied to the limb, it is still less likely to occur.

Whenever digitalis fails, before condemning the drug, one should drain all of these locations, chest, abdomen, skin and bowels, as frequently no physiological effect is apparent until the edema has been partially relieved by such physical measure.

VENESECTION.—This is indicated in any case of sudden marked cyanosis and evident right heart-failure. In a case with high blood-pressure, presenting any symptoms, not reacting to or relieved by ordinary measures, from one pint to one quart of blood should be withdrawn. The most satisfactory technic is as follows: After the site at the bend of the elbow has been cleansed, a bandage is tied about the arm, which is allowed to hang down in order to distend the veins, and an incision is made along the side of the most prominent vessel at the bend of the elbow. The knife is inserted under the vein and it is cut outward.

PRACTICE OF MEDICINE—TICE

☛ Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.

Bleeding by means of an intravenous needle to which a rubber tube is attached eliminates the sight of blood and extravasation, but the author has not found this method satisfactory, unless a large needle such as is used in the transfusion of blood is employed and such a needle is seldom handy. In case it is used, it should be directed from above downward. Cocain is seldom necessary. If the cuff of an ordinary blood-pressure instrument is applied about the arm, and air pumped in to a point midway between the systolic and diastolic pressure and kept there, the flow of blood is more satisfactory than when an ordinary tourniquet is employed.

Rest in Bed.—The patient must remain in bed until all of the demonstrable effusions in the serous cavities have disappeared, and the edema has left the extremities and the dyspnea is not produced on slight movement in bed. A good plan is to wait a week after the edema has disappeared from the legs, before allowing the patient to leave the bed. In the meantime, during treatment, the patient should be instructed to make up and down movements of the extremities for a period of five minutes, three or four times daily. When he does get up, he should be warned of the likelihood of vertigo, which is common in any one who has remained in bed for several days. After recovery to the point to be able to get about without dyspnea or edema, the patient is by no means able to go back to work, if it entails much physical labor. Two or three weeks should be spent in convalescence. As soon as the immediately serious symptoms are on the wane the information should gradually be imparted to the patient that he will certainly have a recurrence of his illness. This must be repeated, again and again, because these patients are naturally optimistic and, when they find themselves apparently free from symptoms, live in a fools' paradise and nearly always think that the ailment has departed, much like any acute infectious disease. It requires some courage on the part of the practitioner to tell the patient, frankly, the exact nature of the remaining lesion, as it takes some of the edge from the thanks and gratitude showered upon him, but it is as necessary as prescribing a medicine. One must be almost brutally frank, especially on the last visit. If the labors of the former occupation were responsible for the ill health, then the patient should be advised to seek a new one, even though it involves a financial loss, because, after all, a year or two of extra life cannot be measured by any financial standard.

If, on the other hand, as is most commonly the case, the break in compensation was due to infection, a change of occupation is not indicated, unless the attack has left the patient unable to perform his former work without the production of symptoms. Finally, it should be impressed upon him as a bounden duty, to return to the physician for a physical examination, at least every two months. It may be argued that there is little change to be detected in the heart itself by such examination, and this is quite true. It is mostly by interrogation as to the presence or absence of symptoms that one can arrive at an estimation of the condition of the heart; but the layman feels that the information gleaned by physical examination is paramount. He thinks that he can judge symptoms for himself. Upon the progression or regression of symptoms between such examinations will depend the necessity of change of occupation and of treatment.

Outline of Treatment for Patient Suffering From One or More of the Marked Symptoms of Decompensation.

First day:

Absolute rest in bed.
Woolen under-clothing.
Blankets.
Hot water bottle to feet.
Nurse ordered to be in constant attendance for one week or more.
No visitors.
Warning to friends as to the seriousness of the condition.
Suggestion that religious and financial matters be broached to the patient by a relative, not by physician.
Reassurance of the patient as to his safety.
Starvation diet for twelve hours.
Dry diet thereafter.
Local applications to chest if needed.
Urine to be measured for twenty-four hours, also fluid intake.
Sample of urine to be sent to laboratory for examination.
If symptoms are severe, hypodermic of morphin, grains ¼ to grains ½ (gram 0.0162 to gram 0.0324) at once; also calomel, grains 2 (gram 0.130), with compound jalap powder, ½ dram (1.95 gram), at bed-time.
Leave following prescription:

℞	Tincturæ opii deodorisati	ʒii (7.50 c.c.)
	Tincture digitalis	ʒiv (15 c.c.)
	Elixir adjuvans	q. s. ad ℥ii (60 c.c.)

Sig.: ʒi (3.75 c.c.) every four hours.

See patient in twelve hours if the symptoms are severe, otherwise next day and each succeeding day until there is some improvement.

In hospital practice, where the decompensation is acute and the patient has not had digitalis, the Eggleston method is a preferable way of administering the digitalis.

Second day:

Dry diet.
No liquids with meals.
Meat, bread, potato, cereal (salt-free).
Liquids, restricted to two pints in twenty-four hours, preferably milk, black coffee or tea.
Continue opium and digitalis.
Aloin or cascara pill at bed-time.
Symptomatic treatment of other complaints.

Third day:

Discontinue opium. If sedative is necessary, use a milder one.
Continue digitalis and other measures as above.

Fourth day:

If there is no decided relief in the presenting symptoms in seventy-two hours, give a Niemeyer pill t.i.d., alternating with diuretin and Karell diet.

Fifth day:

If no results are obtained, paracentesis of cavities and tissues must be seriously considered. If after two weeks there has been no decided improvement, it is well to fortify one's self by calling in counsel. It is only natural that friends of the patient wish a change by this time, and unless something is done, the practitioner is likely to be supplanted; furthermore, the magical change that sometimes takes place in the patient's condition within a day after a consultation, even though there has been no change in medication, is sufficient excuse for the procedure. It can only be explained by the basis of renewed hope and additional determination to recover.

Anders. Practice of medicine. 13th Ed., 1917. W. B. Saunders & Co., Phila.

Abrahams, R. Elements of prognosis in chronic valvular disease of the heart. N. Y. State Jour., April, 1910, iv, No. 4, p. 175.

Boose, N., and Marks. The use of digipuratum in heart disease. Arch. Int. Med., April, 1911, vii, 551.

Broadbent, W. H. Heart disease. 4th Ed. Balliere, Tyndall & Cox, London.

Brooks, H. Syphilis of the heart. Inter. Clinics, 1915, i, Series 25, p. 134.

Brown, P. K. Artificial Nauheim baths in chronic heart disease. Boston Med. and Surg. Jour., 1906, clv, 276.

Bruce. The principles of treatment and their applications in practical medicine. 1912, Lea Bros. & Co., Phila.

Brunton, T. Lauder. Lectures on the action of drugs. 1897, 1st Ed., p. 368. MacMillan & Co., London.

Cabot. The association of diastolic murmurs with mitral stenosis. Trans. Assoc. Amer. Phys., 1914, xxix, p. 22.

Coombs, Carey. Index of prognosis. 1st Ed., 1915, p. 356. Wm. Wood & Co., New York.

Cushney, A. R. Pharmacology and therapeutics. 5th Ed., 1910. Lea & Febiger, Phila.

Dieulafoy. Practice of medicine. 2d Ed., 1912. D. Appleton & Co., New York.

Eggleston, C. Digitalis dosage. Arch. Int. Med., 1915, i, 1.

——— Some newer concepts in digitalis therapy. Am. Jour. Med. Sc., cix, No. 5, p. 625; also Jour. Am. Med. Assoc., March 13, 1920, lxxiv, 733.

Elsner. Monographic medicine. 1916, 1st Ed. D. Appleton & Co., New York.

Epstein, J. Arch. Diag., Jan., 1917, x, 59.

Fontane, S. W. Statistics of frequency of syphilis of the aorta. So. Med. Jour., June, 1918, xi, 278.

Gerhardt. Die Klappenfehler. Wien. 1913.

Gibson, G. H. Diseases of the heart and aorta. 1885, 3d Ed. Macmillan & Co., New York.

Goodman. Mitral stenosis. Am. Jour. Med. Sc., 1919, Nos. 1, 2, and 3.

Hale, W. The comparative strength of digipuratum and a comparative study of digalen. Jour. Am. Med. Assoc., Jan. 1 and Jan. 8, 1910, liv, No. 2, pp. 129 and 351.

Hatcher, R. A., and Brody, J. G. The biological standardization of drugs. Am. Jour. Pharm., 1910, lxxxii, p. 360.

Hirschfelder, A. D. Diseases of the heart and aorta. 1919, 3d Ed. Lippincott & Co., Phila.

Libman, E. Classification of the cardiac murmurs. Med. Clin. North Am., Nov., 1917, i, No. 3, p. 573.

Longcore, W. The relation of the origin of aortic insufficiency to syphilis. Arch. Int. Med., Jan., 1915, xi, 14.

Matthew. Vasodilatation in high blood-pressure. Quart. Jour. Med., April, 1909, ii, 261.

McKenzie. Diseases of the heart. 1917, 3d Ed. Oxford.

——— Symptoms and their interpretation. 1918, 2d Ed. Oxford.

McCallum and McClure. Artificial lesions of the mitral valve. Johns Hopkins Hosp. Bull., 1906, xlvi, 260.

Moon. The prognosis and treatment of diseases of the heart. 1st Ed., 1912. Longmans, Green & Co., New York.

Neuhof and Selian. Clinical cardiology. 1917, 1st Ed. Macmillan & Co., New York.

Norris, G. U. Studies in cardiac pathology. 1917. W. B. Saunders & Co., Phila.

Norris, G. U., and Landis, H. R. W. Diseases of the chest and the principles of physical diagnosis. 1917, 3d Ed. W. B. Saunders & Co., Phila.

Norris and Peterhof. The topography of the cardiac valves as revealed by the x-ray. Am. Jour. Med. Sc., 1915, cxlv, 225.

Pardee, H. Am. Jour. Med. Sc., Nov., 1920, lxxv, 1258.

Pitt, N. Tricuspid disease in Albutt's system of medicine. 2d Ed., 1919.

Sansom. The signs of diseases of the heart and thoracic aorta. 1892, 3d Ed. A. E. Griffin & Co., London.

Sears. St. Paul Med. Jour., Mar., 1917, iv, 272.

Slemmon and Goldsborough. The influence of pregnancy and labor on the heart. Johns Hopkins Hosp. Bull., 1908, xix, No. 208, p. 194.

Stewart. Hypertrophy of the heart. Arch. Int. Med., 1908, i, No. 1, p. 102.

PRACTICE OF MEDICINE—TICE

☛ **Remove from your Vol. VI pages 163–204, inclusive. Insert therefor these New Pages, 163–204.**

TALLEY. Some criteria underlying prognosis in certain forms of cardiac insufficiency. Penn. Med. Jour., Feb. 16, 1919, xix, 338.
THORNE, L. The Nauheim treatment. 5th Ed., 1918. Balliere, Tyndall & Cox, London.
TICE, F. The clinical determination and significance of some of the peripheral signs of aortic insufficiency. Ill. Med. Jour., Sept., 1911, xx, 271.
WARTHIN. The persistence of active lesions and spirochetes in the tissues of clinically cured and inactive syphilis. Trans. Assoc. Am. Phys., 1914, xxix, 417.
WIGGERS, C. J. The circulation in health and disease. 1915. Lea & Febiger, Phila.
WILLIAMSON, C. F. Forchheimer's Therapeusis of heart disease. 1914. D. Appleton & Co., New York.

CHAPTER IV

DISEASES OF THE PERICARDIUM

FREDERICK TICE, M.D., F.A.C.P.

Pericarditis, p. 205:—Definition, p. 205; Etiology, p. 206:—Bacteriology, p. 208 —Clinical varieties, p. 208:—Acute plastic pericarditis, p. 208:—Symptomatology, p. 208:—Clinical history, p. 208:—Pain, p. 208; Fever, p. 209; Palpitation and dyspnea, p. 209—Physical findings, p. 209:—Auscultation, p. 209; Palpation, p. 210—Diagnosis, p. 210—Pericarditis with effusion, p. 210:—Etiology, p. 210 Symptomatology p. 210:—Clinical history, p. 210; Physical findings, p. 211; Roentgen examination, p. 213:—Diagnosis, p. 215—Clinical varieties of acute pericarditis, p. 216:—Pericarditis sicca, p. 216; Serofibrinous pericarditis, p. 216; Purulent pericarditis, p. 216; Hemorrhagic pericarditis, p. 216; Tuberculous pericarditis, p. 217; Luetic pericarditis, p. 217—Chronic pericarditis, p. 217—Treatment, p. 217:—Paracentesis pericardii, p. 219; Course, duration and termination, p. 221; Prognosis, p. 221; Morbid anatomy, p. 222; Pathological physiology, p. 223.
Adherent pericardium, p. 224:—Synonyms, p. 224; Definition, p. 224; Etiology, p. 224; Symptomatology, p. 224:—Physical signs, p. 225; Roentgen examination, p. 227—Diagnosis, p. 228; Treatment, p. 228:—Medical, p. 228; Surgical, p. 229—Prognosis, p. 229; Morbid anatomy, p. 231:—Pericardial lesions, p. 231; Mediastinal and neighboring tissue lesions, p. 231; Cardiac lesions, p. 231; Hepatic lesions, p. 232—Pathological physiology, p. 233.
Hydropericardium, p. 234:—Definition, p. 234; Etiology, p. 234:—Symptomatology, p. 234:—Physical signs, p. 235—Diagnosis, p. 235; Treatment, p. 235; Prognosis, p. 235.
Hemopericardium, p. 235:—Definition, p. 235; Etiology, p. 235; Symptoms and signs, p. 236; Diagnosis, p. 236; Treatment, p. 236: Prognosis, p. 236; Morbid anatomy, p. 237.
Pneumopericardium, p. 237:—Definition, p. 237; Etiology, p. 237; Symptoms and physical signs, p. 238:—Roentgen examination, p. 238—Diagnosis, p. 239; Treatment, p. 239; Prognosis, p. 239; Morbid anatomy, p. 239.
Neoplasms of the pericardium, p. 240:—Malignant neoplasms, p. 240:—Symptoms and physical signs, p. 241; Diagnosis, p. 241; Treatment, p. 241; Prognosis, p. 241—Benign neoplasms, p. 241.
History, p. 241; Bibliography, p. 242.

PERICARDITIS

Definition.—Pericarditis is an inflammatory involvement of the pericardium, either as a primary clinical entity or secondary to some other disease.

In some instances the inflammatory process may be limited to the pericardial sac, as determined by the predominating clinical symptoms and signs, or by the anatomical findings; more frequently there is an associated myocarditis, an endomyocarditis, or the external surrounding structures of the pericardium are also involved. In discussing the etiology of pericarditis, Sibson makes the following statement, "Inflammation of the surface of the heart and the lining of the pericardial sac occurs so very rarely by itself that we cannot practically regard it as a distinct disease."

Von Jurgensen, in his article on endocarditis, without reference to the etiology, but considering chiefly the local anatomical changes, uses the expression "Pancarditis"—and this will be the diagnosis of the future. But he who makes this diagnosis must know how to distinguish the various parts which compose the whole, and to weigh the relative importance of each. The object should be, of course, in each individual case to analyze the composite picture of pancarditis with its constituents—endocarditis, myocarditis and pericarditis.

Etiology.—For many reasons a bacteriologic classification is the ideal one, but this is not possible at the present time. The subdivision of acute, subacute and chronic is not satisfactory, or acceptable, for an etiologic basis, as it applies to the clinical course and renders no assistance as to the actual cause. The old classical and generally accepted classification of primary idiopathic and secondary pericarditis is open to suspicion and doubt, more so with the increased and growing knowledge of the bacteriology of pericarditis, the modes of infection and the associated pathology. While it must be admitted that a primary idiopathic pericarditis is possible and may occur, the frequency of such is gradually decreasing; even the causative factors previously accepted are losing their significance except as contributing factors. Exposure to cold, and trauma have been accepted as potent factors in the production of idiopathic pericarditis, but bacteriology has deprived them of much of their previously accepted influence. No doubt, in some instances, they have an indirect or contributing influence in reducing the general or local resistance, as occurs in many other diseases, but they can hardly be accepted as the primary essential cause. Too often careful examination reveals some obscure focal infection, such as small imbedded but infected tonsils, a pyorrhea with infected teeth, an infected gall-bladder, tracheobronchial adenitis, or pulmonary infection, perhaps without clinical symptoms,—conditions whose significance until recently was underestimated. Even where it is impossible to detect clinically some focus of infection, the anatomical examination demonstrates the presence of tubercles or the presence of organisms.

Secondary pericarditis may occur in practically any infectious disease, the infecting organism reacting on the pericardium due to a systemic infection or by direct extension by contiguity.

Of the primary diseases with which pericarditis is most frequently associated, rheumatism stands preëminent; it is quite analogous to endocarditis. Statistics are variable, but age plays an important rôle. In the young, not only the endocardium, but the myocardium, are prone to infection; in the adult, the joints alone may be involved. Pericarditis usually occurs as a complication of the rheumatic infection, during or subsequent to the arthritic manifestations, but, not infrequently, the pericardial involvement occurs as the initial disease and the arthritis develops later. A proper appreciation of the importance and etiologic relation of rheumatism and pericarditis may be had in a review of the literature.

In 326 cases of rheumatism, Sibson found a pericarditis in 63; Latham reports 7 in 136; while other authors state that it occurs in from 30 to 50 per cent. of rheumatism. Of the 94 cases of pericarditis observed in the County Hospital, 30 occurred as a complication to articular rheumatism. The severity of the infection as well as the duration of the attack is of some importance. Due to the lowered general and local immunity, the pericarditis frequently appears at the height of the infection but it is not uncommon in the recurring, subacute exacerbations of the arthritis. Males are relatively more prone to rheumatic pericarditis, due no doubt to the influence of occupation and greater exposure to contributing causes. Tonsillitis must be considered a close rival of rheumatism; perhaps the former even outranks the latter if the primary or focal infection in rheumatism be considered as a separate disease. The tonsil, with or without clinical symptoms, due to the investigations in local infection, is rapidly becoming more and more incriminated. Chorea, particularly in children, accompanying or following a tonsillitis or arthritis, is a fairly frequent cause. This might be suspected in the light of the investigations of Poynton and Paine, as well as subsequent workers, that all these diseases have been associated with the same organism.

A general sepsis, either primary or secondary, or a pyemia from any form of infection, is a fruitful cause. To this group belongs the systemic infection accompanying pneumonia and typhoid fever, the former a frequent cause of pericarditis, the latter rarely producing pericardial involvement. Luetic infection must be mentioned among the possibilities, but how frequently this is a cause has not been determined Of the eruptive fevers, scarlet fever deserves special mention; less important are measles and small-pox. Diphtheria may act as a cause, but the associated mixed infection is usually the exciting factor.

Tuberculosis of the pericardium as a primary disease is extremely rare, but it has been reported by Scaglios in a personal observation; he also refers to 7 similar cases.

Gonorrheal infection is by no means a rare cause of pericarditis. Most frequently the pericardium becomes involved, accompanying or following a previous complication, such as a gonorrheal arthritis, endocarditis, or prostatitis.

Chronic wasting diseases, such as nephritis, diabetes, carcinoma, and aortic aneurysm, constitute a well-recognized group, frequently complicated by a pericarditis and often terminal.

In the group of diseases producing pericarditis by extension by contiguity, pneumonia and pleurisy are the most frequent, and, in the order of importance, rank next to the rheumatic infections. Pericarditis is a more frequent complication of infection of the right lung than of the left; this is also true in a pleurisy. Chatard reports the findings in 31 of Osler's cases, in which pneumonia was right-sided in 13, left-sided in 5, and bilateral in 13. Of the 29 fatal cases, a pleurisy was present in 28, of which 13 were right-sided, 8 left-sided and 7 bilateral.

Undoubtedly a certain proportion complicating a pneumococcal pneumonia and pleurisy is due to the systemic infection, with a localization in the pericardium, and not necessarily the result of direct extension.

Pericarditis is frequently due to a tuberculous infection, associated with some clinical type of a tuberculosis. Clinically, the pericarditis may appear as the chief manifestation, but anatomically it is secondary to a tuberculous lung, pleura, tracheobronchial glands, or only to the pericardial portion of a general polyserositis. A miliary tuberculosis of the diffuse or pulmonary type may involve the pericardium. A caseating tracheobronchial gland is relatively a frequent form of tuberculosis with pericarditis, especially in childhood and early adult life.

As previously indicated, a pericarditis may constitute only a portion of a more extensive anatomical involvement such as occurs in the various infections producing an infective endomyopericarditis—the pancarditis of von Jurgensen. It is this form of cardiac disease which is so frequently observed in early life; it is due to a rheumatic infection. The same condition may occur in the adult, but it is due more frequently to a pneumonia, sepsis or gonorrhea.

Other forms of infection in the neighborhood of the pericardium may extend and result in a pericarditis.

Pleural empyema, a simple or suppurative mediastenitis, caries of the spine or ribs and pulmonary abscess and gangrene are occasional causes. Coronary thrombosis and emboli, particularly the infective variety, may be productive of pericarditis.

Bacteriology.—As pericarditis is most frequently only an incident or complication in the course of some other acute or chronic disease, the exciting organism will usually depend upon the primary form or focus of infection. The pyogenic cocci, pneumococcus, streptococcus, and the tubercle bacillus are the most frequent, but practically any organism may be present. In some of the acute infectious diseases or in the chronic wasting disease, secondary infections occur and are responsible for the pericarditis. Terminal infections, with lowered resistance, are frequent and probably account for the relative frequency of pericarditis, irrespective of the primary disease.

For convenience of clinical description acute pericarditis may be subdivided into the acute plastic pericarditis and pericarditis with effusion. The plastic character may predominate and little or no fluid exudate may take place, but more frequently the process gradually changes in form from a plastic type to one with an effusion,—the two clinical types representing only a clinical and anatomical variation in the course of the same disease.

Clinical Varieties—Acute Plastic Pericarditis.—(I) *Symptomatology.*—(1) *Clinical History.*—There are no characteristic symptoms; in fact, not infrequently, all symptoms are wanting and the clinical recognition depends upon physical findings, or its existence is unsuspected during life and discovered only at autopsy.

(*a*) *Pain.*—The one and most suggestive symptom is pain, which may be a dull aching character in the region of the heart, or it may be sharp, excruciating, and localized to the cardiac region or referred to the left shoulder and arm, not unlike the pain in an angina pectoris. In the course of some other acute infectious disease, discomfort or actual pain in the cardiac region should arouse suspicion of acute pericarditis and lead to a careful examination. When the pain is of the anginoid type, particularly with the dolor pectoris element without the angor animi, and when it is constant or prolonged, pericardial involvement should be suspected. In more than one instance, with these conditions present, a tentative diagnosis of acute pericarditis was made, even when the physical signs were yet uncertain.

(*b*) *Fever.*—Fever, like the pain, may or may not be present. In the infective type there is usually some elevation, as might be expected, but how much is due to the primary disease and how much to the complicating pericarditis is not easy or possible to determine. When present, the fever is usually moderate in amount except in the very acute or severe forms, depending upon the type of infection and the primary disease. The acute plastic pericarditis, so frequently encountered in the aged, or as a terminal manifestation, is usually fever-free.

(*c*) *Palpitation and Dyspnea.*—Palpitation and dyspnea are also extremely variable, frequently entirely absent, and more indicative of an associated valvular or myocardial lesion.

(2) *Physical Findings.*—(*a*) *Auscultation.*—The recognition of an acute plastic pericarditis usually depends upon a thorough physical examination and the detection of the characteristic, practically pathognomonic, ausculatory, to-and-fro friction rub; the "squeak of the leather of a new saddle under the rider" was first described by Laennec and ascribed to pericarditis, but later he changed his opinion. Subsequently, Collin, in 1824, again definitely declared that the "pericardial rub" is a sign of pericarditis, but he erroneously believed that it was produced by a dryness of the sac. The chief and determining characteristics of this pericardial rub are its great irregularity and variability, not only in rhythm but in time, intensity and audibility. The pericardial rub depends upon the rough, irregular surface of the pericardial surfaces, due to the fibrinous exudate, and the cardiac action. In general, the friction rub is systolic and diastolic, corresponding to the cardiac cycle, but the sounds are not synchronous. The friction rub may accompany, precede or follow the cardiac sounds; it is usually double, systolic and diastolic, but occasionally it is single or even triple, and suggests an irregular shuffling sound. It may appear early in the disease, persist for a variable period or recur from time to time with subsequent examinations.

A few hours or minutes may suffice for it to disappear or reappear. More than once, it has been impossible to demonstrate in the clinic a pericardial rub which was present in the ward but a short time before. The very reverse is equally true. This variability may, in part, depend not only upon the amount and character of the exudate but, to a greater extent, upon the cardiac action and force. When doubt exists as to the presence of a rub, a few deep breaths or slight exercise,such as sitting upright or a change of posture, may suffice to intensify the findings and remove all doubt.

The rub may be audible over the entire precordia; perhaps it is transmitted beyond for a limited distance, but it possesses no definite line of transmission as in endocardial murmurs. More frequently it is localized or heard with maximum intensity over certain areas, especially at the right ventricle, at the base, or (rarely) at the apex. Intensity of the rub may be varied by the amount of pressure with the stethoscope.

(*b*) *Palpation.*—Palpation sometimes reveals the presence of a friction fremitus, but it is of relatively little assistance except in conjunction with auscultation. Inspection and percussion are negative in this type of pericarditis, unless they are associated with some other involvement.

(II) *Diagnosis.*—Recognition of pericarditis in this type of the disease is rarely difficult. The pericardial rub is so distinctive, when once heard, that there can be no doubt. Conditions, however, may exist and render a diagnosis questionable or impossible. Lobar pneumonia, a chronic renal lesion with coma, acute cardiac involvement or some other disease, complicated with acute pericarditis, may so mask or obscure the physical findings that it passes unrecognized. This has occurred, particularly in the pneumonia patients, when admitted in the terminal stage; dyspneic compensation failed and the lungs filled with large moist râles.

A pleuropericardial rub, due to a pleurisy, can usually be differentiated, as it is more definitely associated with the respiratory action than it is with the cardiac action; and it is heard with maximum intensity along the left border of the heart and lessens or entirely disappears when the patient suspends breathing. Further evidence of a left-sided pleurisy, plastic or with an effusion, may be present and will be of assistance.

When the pericardial rub is double, with maximum intensity over the base, and accompanying the cardial tones, it may simulate or suggest a double aortic valvular lesion. Little or no difficulty need occur here in diagnosis as an appeal to the peripheral vascular signs will at once render a decision possible.

A single systolic, pericardial rub localized at the apex may suggest a mitral regurgitation, but differential diagnosis is made possible by negative cardiac signs in pericarditis, and repeated auscultation will usually reveal lack of synchronism or an occasional double rub.

Reference should be made to the possible existence of a pericardial rub, due to a dryness of the sac in dehydrated conditions, as described by Pleisch in cholera, where no actual inflammation can be demonstrated. Admitting this possibility, there is no convincing proof that such is the case, while it is more plausible that the rub is due to structural changes, produced by infection or retained toxins.

PERICARDITIS WITH EFFUSION.—When the fibrinous exudate, in the acute plastic type, fails to undergo absorption or organization, an effusion may take place. Depending upon various factors the effusion or exudate may assume the serofibrinous, hemorrhagic or purulent form, the occurrence of which, in an acute plastic pericarditis, is so frequent that it is often designated as the second stage of an acute pericarditis.

(I) *Etiology.*—The same factors are present which are found in the acute plastic type. Rheumatism and rheumatic infections, pneumonia, tuberculosis and the septic infections should have special mention. The hemorrhagic form is not infrequently due to a tuberculosis, malignancy, aortic aneurysm, a chronic nephritis, or to the so-called hemorrhagic diathesis.

(II) *Symptomatology.*—(1) *Clinical History.*—As this form usually follows the acute plastic pericarditis, the onset and clinical course, in the beginning, is quite similar. In some the onset is slow, insidious, and without any complaint referable to the heart, even when the pericardium is enormously distended. Pain, fever, dyspnea and compression symptoms predominate and are the most important. In the developmental stage, pain and discomfort of the character encountered in the plastic form are present. As the fluid exudate increases, the pain usually decreases and dyspnea becomes more pronounced, although in individual cases the latter condition may be remarkably slight. At first the patient may rest best in the recumbent position, but as the dyspnea increases, he will insist on sitting upright or on leaning forward.

Distention of the cervical veins and cyanosis may be a marked feature associated with the dyspnea, being partly due to the exudate mechanically interfering with the cardiac function and partially due to the compression of the left lung in massive effusions.

The radial pulse is often irregular, soft and compressible, perhaps rapid and occasionally of the pulsus *paradoxus type,* although this is more constant in the obliterated form of pericarditis. Other compression symptoms consist of dysphagia, aphonia, cough, and pupillary disturbance such as is observed in aortic aneurysm.

(2) *Physical Findings.*—(*a*) *Percussion.*—The pathognomonic signs of pericardial effusion will be determined chiefly by percussion and auscultation. As the fluid exudate increases, and distends the sac, the normal cardiac dulness gradually becomes altered, assuming an abnormal outline with changes in the cardiac sounds. Skoda has directed attention to the accumulation of the effusion in beginning pericarditis at the base of the heart, due to the less intimate contact, to the greater laxity of the sac about the great vessel, and to the lighter gravity of the effusion as compared to the heart. Due to the limited space, distention of the cardiac portion of the sac occurs as the effusion increases. This may take place laterally, posteriorly, or in all directions, depending upon the amount of the fluid; it produces the physical signs characteristic of the disease.

Relatively early Epstein's cardiohepatic angle becomes dull; this condition was first described by Rotch. This may be increased by having the patient lean forward and to the right. Epstein also directed attention to the gradual change from a right angle to one more and more obtuse. When the distention is sufficient the normal cardiac dulness is no longer present with the base directed upward but becomes pear-shaped with the base downward. This area of dulness is so characteristic of pericardial effusion that it is practically a pathognomonic sign.

Long ago Skoda called attention to the influence of change of position of the patient on the shape and boundaries of the area of dulness. The distended pericardium behaves very much like a partially filled rubber bag. When the patient is sitting upright, the base is increased; when leaning forward, the area of dulness is greater; while the lateral posture produces a shifting to the corresponding side. Shattuck more recently has described and emphasized the clinical importance of the same percussion findings.

With the distention of the sac, the pulmonary borders are pushed aside, particularly the left, with frequently a Skoda's resonance in the left axillary area.

Almost constantly, the lower lobe of the left lung presents evidence of varying degrees of compression. This may be slight and limited to a small area below and to the inner side of the inferior angle of the scapula as described by Ewart and Pins.

Localized dulness, with bronchial breathing, is usually present. In many instances the entire left lower lobe presents the findings suggestive of consolidation with the diagnosis of lobar pneumonia. Dulness, or even flatness may be present over the posterior left chest from the interlobar fissure to the base. Bronchial or tubular breathing and bronchophony, usually without râles, are associated findings.

With these pulmonary signs, a careful examination should be made to determine the presence of a pericarditis with effusion. So suggestive are the findings that it has been possible, in several instances, to diagnose a pericarditis even before other pericardial signs were present or could be convincingly determined.

While the. distended pericardial sac, with the resulting compression, is sufficient to produce the pulmonary signs, in some cases the findings are due to an accompanying pleurisy with effusion. This has been determined by puncture and aspiration of the pleural fluid, the compression findings becoming less marked or disappearing entirely.

(*b*) *Auscultation.*—The auscultatory findings in pericarditis with effusion will vary with the stage of the disease. A rub can usually be detected before the effusion has become marked, but even then it is often audible over some circumscribed area of the pericardial dulness. In pleurisy with effusion, the rub disappears as the inflamed and fixed layers of the pleura are no longer in contact, but in pericarditis with effusion the conditions are different. The heart is relatively free, being suspended in the effusion, and when the myocardium has retained sufficient power, it is forced during systole through the fluid and comes in contact with the parietal layer of the pericardium. As the myocardium weakens or as the effusion becomes massive, the rub may no longer be heard. Detection of the rub is always of the greatest importance in the matter of diagnosis. Equally significant is the character of the cardiac tones and their gradual muffling or disappearance with subsequent examinations.

(*c*) *Palpation.*—Palpation, as emphasized by Skoda, may be of considerable assistance in determining the location of the apex beat in relation to the left border of the pericardial dulness. When present, it will be found well inside of the area of dulness. Frequently, however, the location of the cardiac apex will depend, not upon palpation, but upon the determination of the point of maximum intensity of the cardiac tones by auscultation.

(*d*) *Inspection.*—Inspection is usually of but limited service, except perhaps in children, where a bulging precordia and obliterated intercostal spaces may be present.

Prominence in the epigastrium has been emphasized by some clinicians as an important sign, due, presumably, to an accumulation of fluid in the dependent part of the sac. Others have described a palpable left lobe of the liver from a downward displacement. Either or both may be present, but they can hardly be considered of much importance, or regarded as early signs. Probably in many instances the epigastric prominence and palpable liver indicate a passive engorgement of the liver from failing cardiac compensation, rather than a pericardial effusion.

It would be impossible to give more explicit or important information as to the method of observation and diagnosis, than that given by Osler: "In every instance, when a pericardial friction murmur has been detected, the practitioner should first outline with care—using the anilin pencil—the upper and lateral limits of cardiac dulness, mark the position of the apex beat, and note the intensity of the heart sounds."

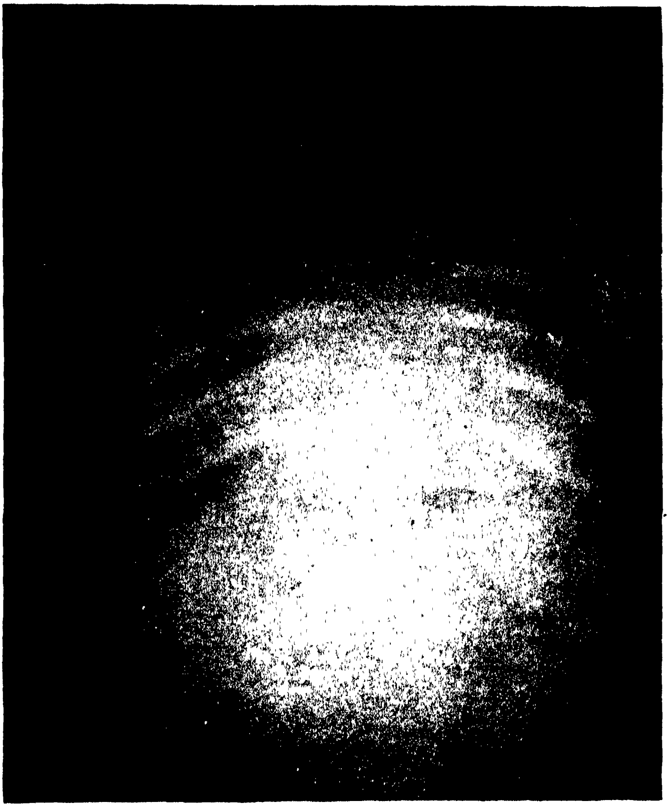


FIG. 1. RADIOGRAM OF PERICARDITIS WITH EFFUSION, DUE TO RHEUMATIC INFECTION.

(3) *Roentgen Examination in Pericarditis with Effusion.*—Roentgen examination may be of the greatest aid in confirming the diagnosis, or it may be of assistance in the differential diagnosis; it may also be a means of determining the relative amount of exudate. In any doubtful case, the physical examination cannot be considered complete without the roentgen findings.

While the literature on roentgen examination and diagnosis in the various fields of medicine and surgery is sufficiently voluminous, relatively little applies specifically to pericardial disease. The recent investigations by George W. Holmes, as contained in his report, are very much to the point and furnish an excellent summary of the subject. Experimentally and clinically, various problems were investigated; this was particularly of service in the clinical diagnosis of pericardial effusion; following is a summary·

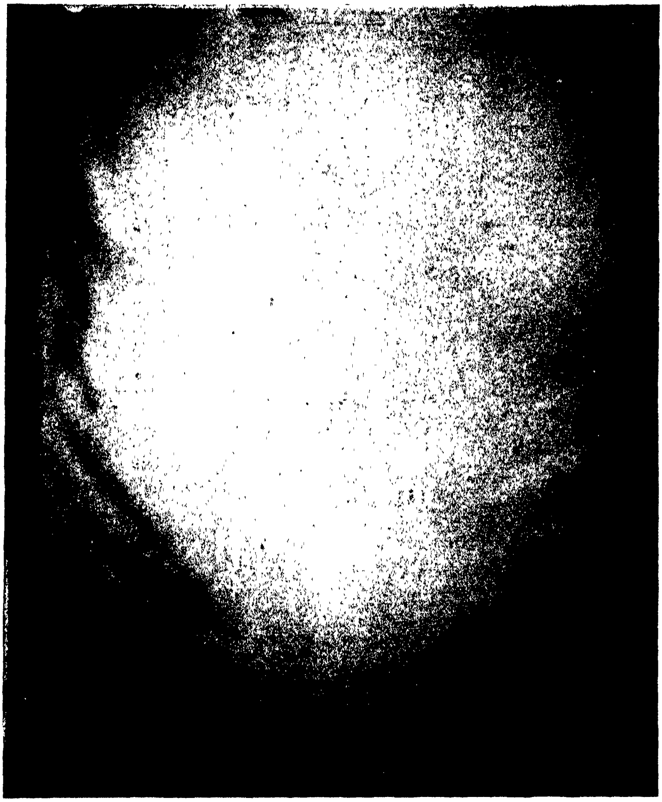


FIG. 2. RADIOGRAM OF PURULENT PERICARDITIS, SECONDARY TO SUPPURATIVE TUBERCULAR CERVICAL ADENITIS.

"In pericarditis with effusion, it seems to me that the findings may be grouped in the order of their importance as follows:

"1. An abnormally shaped heart shadow which changes with change of position of the patient. (So far as my observations go, this sign is not present in any other condition.)

"2. Obliteration of the normal heart outline.

"3. Change in shape of the angle formed by the posterior border of the heart, the diaphragm, and the spine.

"4. Faint or absent pulsation."

Years ago, Francis Williams recommended the examination of the patient in the sitting and recumbent positions, changing from the dorsal to the right and left sides, in order to determine any modification in the heart shadow. Examined in the upright position, the effusion produces the characteristic "pear-shaped" shadow and obscures the normal cardiac contour.

Absence of pulsation speaks strongly for effusion, although in limited exudates a slight transmitted pulsation may be present. In widely dilated, decompensated hearts, there may be little or no pulsation but the outline of the shadow, lack of influence on change of position, and difference in the angle formations will assist.

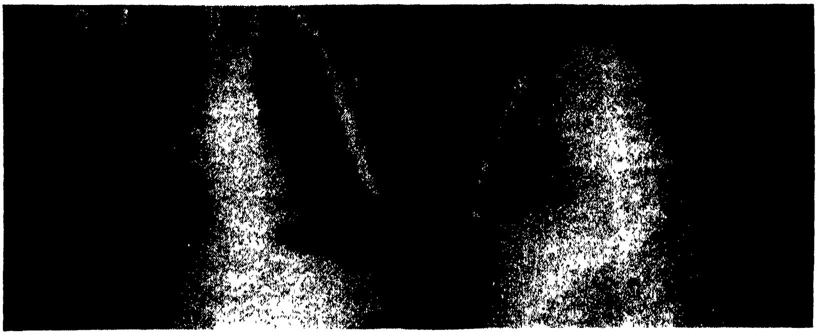


Fig. 3. Radiogram of Pericardial Effusion in an Infant, Showing Shifting of Fluid, Due to Change of Posture of Patient. First Picture, Patient was Recumbent with Face Downward; Second Picture, Patient was Upright.

Williams, Holmes, and others are all practically agreed that it is impossible by roentgen examination to determine the character of the effusion.

(III) *Diagnosis.*—The recognition of a pericarditis with effusion is not difficult, if the case has been under observation from the onset, and there has been the necessary care and repeated examinations. If examined for the first time, when the effusion is already present, particularly when complicating some other disease, pericarditis is often overlooked or misinterpreted. This is abundantly proven by the autopsy records in any hospital with a sufficient amount of material.

Undoubtedly the greatest difficulty, and the largest number of mistakes occur in the differential diagnosis between a pericarditis with effusion and cardiac dilatation. Theoretically this is easy; any senior student or member of a hospital quiz class can readily give a complete list of differential points, but, when applied clinically, there exists a wide difference filled with difficulty.

A recapitulation of the physical signs, which should be of service, may be made as follows:

1. The triangular, "pear-shaped" area of dulness, with the apex directed upward, speaks for pericardial effusion.
2. Visible, palpable or ausculatory apex beat inside the area of dulness has the same significance.

3. Gradually diminishing intensity, muffling or absence of the heart tones indicate effusion, unless the myocardium is greatly weakened. In dilatation, the tones are sharp and distinct; the rhythm is often disturbed.
4. A pericardial rub, even transitory, over any portion of the area of dulness is a most important finding in favor of pericarditis.
5. Rotch's sign, dulness in the cardiohepatic angle, is of value when combined with other findings.
6. As described by Epstein, effusion produces an obtuse cardiohepatic angle, while cardiac dilatation produces a right angle.
7. Compression of the lower lobe of the left lung, producing the sign of Ewart and Pins, is almost always due to effusion. Only very rarely does it result from cardiac dilatation, as determined at autopsy.
8. Visible cardiac impulse is usually absent in effusions and present in dilatation.
9. Palpatory impulse and shock of the cardiac sounds occur more frequently in dilatation.
10. Roentgen examination is often of the greatest service.
11. In doubtful cases, the exploratory puncture will eliminate any question of doubt.

Even after the most careful physical examination, a definite diagnosis may not be possible until exploratory puncture is made. A differential diagnosis between effusion and dilatation has been one of the most difficult clinical problems; in many instances where effusion was suspected, only a dry puncture was obtained.

Left-sided pleurisy with effusion, displacing the heart to the right, will cause but little difficulty when the signs are carefully determined. Usually the two diseases are sufficiently distinct and little or no confusion exists.

Pneumonia with pericardial effusion presents far greater difficulty, not only in determining its presence but in estimating the amount of the fluid. Generally there is a far greater quantity than is suspected, as the pleuropneumonia prevents or interferes with any accurate estimate.

CLINICAL VARIETIES OF ACUTE PERICARDITIS.—*Pericarditis Sicca.*—This type is a dry plastic, fibrinous pericarditis, characterized anatomically by a predominance of the fibrinous exudate which may be circumscribed or diffuse; it is clinically manifested by symptoms as previously described and by the pathognomonic physical sign—the pericardial rub.

Serofibrinous Pericarditis.—This is the most frequent form of pericarditis with effusion, occurring usually as the second stage of a dry pericarditis; it is secondary to rheumatic infections but occasionally it develops as a primary lesion.

Purulent Pericarditis.—This form may occur secondary to the plastic or serofibrinous type, the exudate gradually changing to the purulent type. More frequently it develops in the course of some pyogenic infection, as a sepsis, pyemia, pneumonia, or some focal infection.

Hemorrhagic Pericarditis.—In this form, the effusion is mainly a blood-stained serum containing little fibrin and only a few leukocytes. Its presence usually indicates a tuberculosis, malignancy, chronic Bright's disease, or some blood disease with a hemorrhagic tendency.

Tuberculous Pericarditis.—This form is due etiologically to an infection of the pericardium with the tubercle bacillus; it usually occurs as a complication in the course of a previous infection of other organs, but it may be primary. Tuberculous pericarditis is capable of producing quite a variety of anatomical changes, some of which are characteristic. The exudate varies from a fibrinous, serofibrinous or hemorrhagic to even a purulent form, such as occurs in other forms. Careful search will often reveal the presence of tubercles or a caseating lesion in proximity to the pericardium, *e.g.*, a tracheobronchial or mediastinal gland. It has been observed at all ages but perhaps more frequently during childhood or early adult life, coincident with the prevalence of infection in the other organs, such as the glands, lungs and pleura. The symptoms and signs are those of a simple ordinary pericarditis and only the latency, the associated clinical disease, or the obtaining of a bloody fluid on puncture, may first suggest the tuberculous origin. Examination of the aspirated fluid may furnish valuable diagnostic assistance.

Luetic Pericarditis.—With the recent development in the knowledge of lues and its etiologic significance in cardiovascular disease, involvement of the pericardium might be considered as a not infrequent occurrence. However this may be, luetic pericarditis, at least up to the present, presents more of an academic interest than of clinical entity.

The increasing frequency with which the spirochæta pallida is demonstrated in cardiac and aortic lesions, would justify the conclusion, or at least give reason for strong suspicion, that the pericardium must also become infected. If it escapes, there may be something in the type of the infection or structure of the pericardium, as the scant vascularity, which renders a relative immunity. Ricord, in 1851, first described the disease; Virchow, ten years later, in 1861, reported the second case. Infection of the pericardium probably occurs soon after the initial lesion, during the period of systemic infection, and it is followed by a chronic process which results in a plastic exudate and adhesions. Gumma of the sac have been described but are relatively rare; a serofibrinous type of the disease is also rare.

Chronic Pericarditis.—In some instances in which there is a mild onset, slight symptoms, and a prolonged clinical course, a designation of chronic pericarditis appears justifiable, particularly in such diseases as carcinoma, tuberculosis, diabetes or chronic nephritis.

Acute pericarditis is often followed by a prolonged convalescence; the acute symptoms gradually disappear, while the physical signs still persist. Chronicity may justly arouse suspicion of a tuberculous pericarditis of a mild unrecognized suppurative type, or of the development of an adhesive pericarditis.

Treatment.—This must necessarily depend upon the form of the disease, the stage of development, the predominating manifestations, and the existing complications. It can hardly be claimed that there is any means at our command to prevent infection of the pericardium. The appropriate therapeutic treatment for the various forms of infection enumerated in the etiology is a matter of fact. Whether the salicylates, or similar treatment, for a rheumatism have any definite influence in preventing a pericardial complication is open to question. It might seem reasonable to believe that the longer the arthritis continues, the greater the danger of complications. While there may be a question on this point, there can be little doubt as to the beneficial effect of **absolute rest** as a preventive measure; this measure is well known and recognized in the prevention of acute endocarditis. Prolonged, absolute rest, not only in acute rheumatism, but in many other acute infections, may be of greater service than can be actually estimated.

When the pericarditis is already present, the therapeutic indications consist in the following: (1) giving the patient relief; (2) combating the inflammation; and (3) preventing the cardiac failure.

Pain and dyspnea, the predominating symptoms, may be sufficient to demand immediate relief. If mild or moderate in severity, the application of an **ice-bag** or **ice coil** may suffice. Some patients will prefer the use of a **hot-water bag** or **electric pad,** but, therapeutically, the application of cold is to be preferred. When the discomfort is pronounced or extreme, **opium** or one of the **opiates** will give relief; these measures may require repeating, as indications demand.

As to the second indication, we are almost as helpless as in the efforts to prevent the infection. Rest, with the application of the ice-bag or coil will be of some service. Many of the methods and drugs recommended are very questionable, more empirical than rational. When one recalls the varied etiology and anatomical changes, it would be hoping for the impossible to expect a cure or even an improvement in certain types, no matter what treatment might be employed. Counter-irritation blisters, antiphlogistics and resolvents, formerly so strongly recommended, have fallen into discredit and find no place in the treatment of pericarditis, unless it be in the stage of effusion. Even then, the beneficial effect is so doubtful as to hardly merit recognition or sanction. The salicylates, alkalies, quinin, atropin, iodids, and a long list of other drugs belong in the same category.

In the rheumatic form of pericarditis, **sodium cacodylate,** hypodermically or intravenously, to full therapeutic effect, is apparently of real value. Repeated use, over a considerable period, has only strengthened the conviction of its efficiency.

The third indication, prevention of cardiac failure, involves several considerations. The main objects to be attained consist (1) in minimizing or removing the mechanical hindrance to the cardiac action—the removal of the pericardial effusion, and (2) in limiting the damage to the heart and reinforcing the myocardium.

Just what factors control the production of an effusion and how they may be influenced or governed, it is impossible to say. The slowing of the heart, due to rest and application of cold, must have a beneficial effect in several ways. The myocardium is subjected to less strain, its contractile power is increased, and the decreased activity must assist in minimizing the tendency to myocarditis, as well as in decreasing the irritation of the inflamed pericardium.

Fortunately the pericardium is readily distensible, permitting a considerable accumulation of fluid before there is sufficient pressure to interfere with the cardiac function. In most cases, watchful expectancy is all that is necessary, as the fluid will gradually disappear. As a matter of fact, little or no result may be had from various therapeutic efforts, short of surgical means. **Rest** in the **semiprone** or **sitting position** to relieve the dyspnea, **free elimination,** and **regulation** of the **diet** are only general measures, dictated by common sense. As for any specific drug therapy, there is none.

When the heart is embarrassed mechanically by pressure of the fluid, **surgical relief** by **aspiration** or **drainage** is necessary. The indications and methods will be described in a subsequent section.

A few statements should be made in reference to the efforts to support the failing heart. Opinions are at variance in the use of digitalis in any form of pericarditis. With due regard and respect to those opposed, **digitalis** has been used with apparent benefit, in both the dry and effusive forms. As in valvular disease, the beneficial effect has been more marked with a rapid, irregular heart. **Strychnia,** as a general muscular stimulant, has been of much service. In acute cardiac disturbance such remedies as **camphorated oil** and **caffein sodium benzoate** should be used.

Paracentesis Pericardii.—**Puncture** of the pericardium may be done either as an aid in diagnosis or for therapeutic purposes. In all doubtful cases, **exploratory puncture** is strongly recommended. Performed with due care, under aseptic conditions, no harm can be done. **Repeated punctures** in the same case may be indicated. By means of the puncture, not only the presence or absence of fluid, but its character, will be determined. It is only by this means, in not a few instances, that a final and absolute diagnosis may be made. This statement applies generally but specifically to the question of cardiac dilatation and pericardial effusion. More than once, after a puncture, it has been necessary to revise a diagnosis of effusion to cardiac dilatation or vice versa.

Obtaining fluid is the best evidence of pericardial effusion and affords the opportunity of further examination by laboratory methods and animal inoculation. As for the **therapeutic puncture,** this is a clinical problem, often most difficult to decide. Certain indications were given by Schuh and Skoda as follows:

1. The vital indications, when the life of the individual is threatened by cardiac failure or dyspnea.
2. When the effusion fails to absorb after prolonged observation, in cases in which other means have produced no effect.

The site of the puncture is not a matter of indifference, as failure may occur or harm may be done. Gumprecht mentions the following considerations:

1. Select a point in the location of the pericardium as determined by the examination.
2. The location of the internal mammary vessels should be avoided.
3. No harm should be done to the pleura.

Not only are these considerations important but also the location of the heart in the pericardial effusion. Skoda was of the opinion that the heart sinks downward in the fluid, because of its greater density. According to the findings of Schaposchnikoff the very opposite is true, *i.e.*, the heart floats in the fluid unless the aorta is weakened and elongated by the inflammatory process. This view was accepted by Romberg, Doebert, Fraenkel and others.

The accompanying illustration will show the various sites which have been selected and recommended for exploratory puncture or aspiration. Everything considered it would seem that the fifth intercostal space, inside of the line of dulness not far from the normal location of the apex beat, is the site to be preferred. In this area, the distended pericardial sac is in close contact with the chest wall, the pleura is pushed aside and if the heart is in contact with the pericardium, little or no harm can be done, as the underlying thick left ventricle is not easily damaged. The author can vividly recall his first puncture in a questionable pericardial effusion or cardiac dilatation. Under the direction and supervision of the attending physician, the needle was inserted in the right fifth intercostal space, close to the sternum. Contrary to expectations, no pericardial fluid was obtained but there was an active spurting of blood; a cardiac, as well as a pericardial puncture had been made, fortunately without any bad results. With the usual and necessary precautions, this could hardly occur when the puncture is made in the normal apical region.

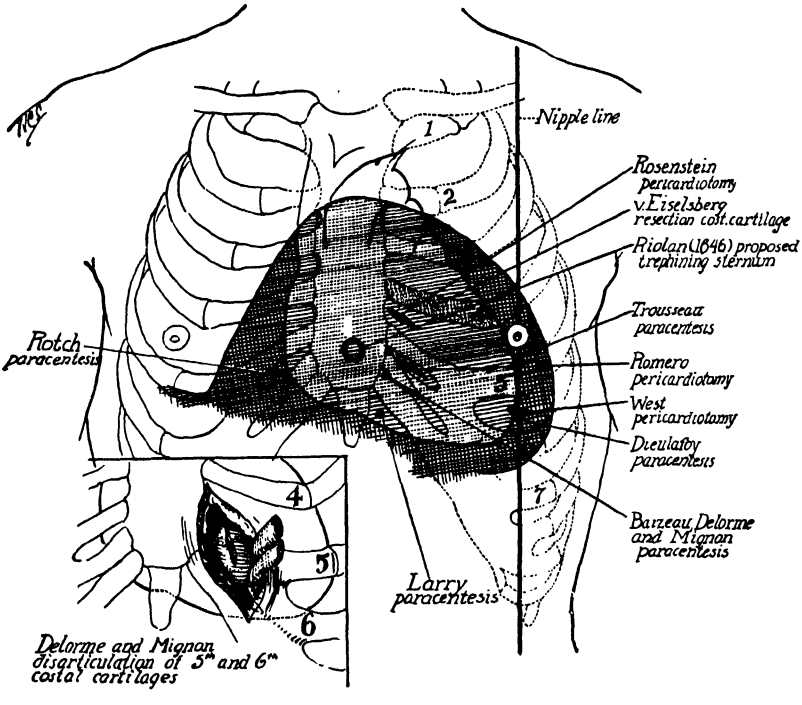

Nipple line
1
2
Rosenstein pericardiotomy
v.Eiselsberg resection cost.cartilage
Riolan (1646) proposed trephining sternum
Trousseau paracentesis
Romero pericardiotomy
West pericardiotomy
Dieulafoy paracentesis
Baizeau, Delorme and Mignon paracentesis
Rotch paracentesis
4
5
6
7
Larry paracentesis
Delorme and Mignon disarticulation of 5th and 6th costal cartilages

FIG. 4. DIAGRAM GIVING THE MORE FREQUENT SITES OF ELECTION IN PERICARDIAL PUNCTURE, ASPIRATION AND DRAINAGE.

In most cases, with the usual physical signs, when puncture is indicated, the site of election is the left fifth intercostal as described. When compression signs are pronounced and doubt exists as to the diagnosis between a simple compression, lobar pneumonia or coëxisting left-sided pleural effusion, the puncture has been made posteriorly in the eighth or ninth interspace, just below and inside the angle of the scapula. If a pleural effusion is found, this should be aspirated and the effect on the symptoms and signs determined. When no pleural fluid is obtained, the needle may be inserted deeper until the pericardium is punctured and then aspirated. After removal of the fluid, compression findings decrease or usually disappear, but if a pneumonia exists, emptying of the sac has no appreciable effect on the pulmonary signs. On a number of occasions the same procedure was employed after removing the fluid in a pleural effusion. The posterior puncture should not be made if there is any suspicion that the pericardial fluid is purulent, if compression signs are absent, or if there is no question as to pleural or pulmonary pathology.

As soon as the nature of the fluid is determined, the further course of procedure is variable. Serofibrinous or hemorrhagic exudates should be aspirated, and as much removed as possible. To assist the flow, the patient may be in a sitting, semi-sitting or lateral position and the fluid removed by siphonage. Usually moderate suction with an aspirating apparatus will be found more practical and oftentimes it is absolutely necessary for a successful result.

If the exudate on exploratory puncture is found to be purulent, aspiration is advisable, but incision and free drainage should be done at once. The same treatment should be employed in protracted, recurring effusions which fail to respond to simple aspiration.

Course, Duration and Termination.—No definite and absolute statement is possible, as the determining factors are too variable. Approximate accuracy may be attained in reference to the course in acute pericarditis, as the plastic type generally becomes changed into a pericarditis with an effusion. The primary disease, of which the pericarditis is only a complication, is often a far more important factor in determining the course, duration and termination than the pericarditis. The plastic pericarditis is usually of short duration, from a few hours to a few days, terminating in recovery or in a pericardial effusion which may run a clinical course of weeks or months. When the plastic exudate is limited, it may undergo absorption and the pericardium return to normal. The so-called "milk-spots" or "soldier-spots" on the heart, so frequently found at autopsy, may be due to a sclerotic thickening of the visceral pericardium, the remains of a previous pericarditis. Almost without exception, the exudate undergoes organization and produces adhesions or obliteration of the sac. When effusion occurs, after a varying period, the fluid is gradually absorbed and the fibrinous portion becomes organized with the pericardial layers adherent. Under the heading of morbid anatomy, reference was made to some of the factors and possibilities in pericardial exudates. The end results in the various forms of acute pericarditis will be described under adhesive pericarditis.

Prognosis.—The prognosis is variable and questionable, depending in part upon the form of the disease, but far more upon the primary disease and the associated pathology. Acute plastic pericarditis, uncomplicated, is never fatal.

The immediate outlook in the serofibrinous form, particularly of the rheumatic type, is favorable; the ultimate outcome, due to cardiac involvement or to the resulting adhesive pericarditis, is often unfavorable.

Myocarditis is practically always present, either as an accompanying cardiac involvement of the same infection, or by extension from the pericarditis. Purulent pericarditis of septic origin is usually fatal, often within a few hours or days. The tuberculous form presents a somewhat better outlook, occupying a prognostic position somewhere between that of the dry plastic and the purulent types.

Pericarditis tends to a fatal termination in the following ways: (1) by mechanically interfering with the cardiac action by the pressure of the effusion or the obliteration of the sac by adhesions; (2) by extension of the inflammation producing a myocarditis; and (3) possibly through the injurious effects from absorption of the toxins. The first mentioned effect is the most dangerous, although the presence of a myocarditis is a serious matter.

After all, a prognosis most carefully determined, based upon all the existing findings, may be upset by the course of the primary disease or by some unforeseen complication, such as an acute endocarditis or embolism.

Morbid Anatomy.—The anatomical changes in a pericarditis are variable, depending upon the exciting organism, as well as upon the local and general resistance. Following the infection, the pericardium becomes lusterless, a leukocytic infiltration occurs, followed by a varying amount of fibrinous or fluid exudate. The exuded fluid is relatively rich in fibrinogen, which undergoes subsequent changes and determines the character of the exudate. Opie is of the opinion that the fibrinogen is acted upon by a proteolytic enzyme, derived mainly from the polynuclear leukocytes. In the presence of the ferment, a fibrinous exudate is formed; when the ferment is absent, the exudate remains fluid. If the organisms are particularly numerous and the leukocytes are abundant, the ferment digests the fibrin and the exudate becomes purulent.

Plastic pericarditis, the usual and most frequent form, may be local or general. As the exuded fluid and leukocytes are given off from the circulation, the fibrinous formation will first appear in the course of the vascular supply of the pericardium and heart. Later the entire surface becomes covered and, when abundant, forms a fibrinous layer with an irregular surface and long shreds—the shaggy-heart or cor villosum. The appearance of the pericardium in this form has been compared to that of two peices of bread and butter pulled apart. The pericardial surface may be covered with a thin uniform layer, but more frequently there is a ridge and furrow formation, due, according to Kornitzer, to the rotary action of the heart during systole.

The plastic form of pericarditis is characterized anatomically by the abundance of the fibrinous exudate, with little or no fluid. After a varying period of hours or days there is an accumulation of fluid, producing a pericarditis with effusion. The rapidity of formation, as well as the amount and the character, are all variable.

Occasionally a dry form becomes converted into one with effusion with surprising rapidity,—within a few hours, and usually within a few days at best. The amount may be limited to a few cubic centimeters, usually from 2 to 300 c.c. (32.4 minims to 10.14 fluidounces), but it may reach or even exceed 2 liters (4.227 pints). At autopsy, Verney removed 4000 c.c. (135.24 fluidounces).

The type of effusion most frequently encountered is the serofibrinous, associated with the rheumatic infections. Less frequently the fluid is hemorrhagic or purulent.

It should be emphasized that an inflammatory involvement is rarely, if ever, strictly limited to the pericardium. The underlying myocardium presents evidence of infection, perhaps only the most adjacent portion, but more frequently it is extensive, involving the greater part, as well as the endocardium—a pancarditis.

The fluid may become sacculated by the fibrinous exudate or adhesions, so that the greater part is found walled off and limited to some particular portion of the pericardium. Multiple pockets may form, particularly in the process of absorption and organization.

Adhesions may form, either cordlike or more extensive, binding together the two layers of the pericardium. This is more frequent in the later stages of the disease, but during the acute and early stage the layers are partially or completely adherent; this is due to the inflammatory exudate.

Pathological Physiology.—The heart, under normal conditions, is suspended at the base by the great vessels, hanging practically free in the pericardial sac. According to Adamkiewicz and Jacobson the normal intrapericardial pressure varies from −3 to −5 mm. Hg. Although the serofibrous structure of the pericardium is such as to permit of considerable stretching, the support given to the heart is of considerable physiological consideration in maintaining a normal circulation. When involved in some inflammatory process, the sac is weakened, more easily stretched and the normal support lessened. In the event of a pericardial effusion, the resulting intrapericardial pressure is exerted not only upon the sac but also upon the heart. The distensibility of the pericardium is of greater importance than the actual amount of contained fluid, so far as symptoms and signs are concerned.

Experimentally François-Franck, Cohnheim, Starling and others have determined by injections into the dog's pericardium, that from 20 to 30 c.c. (5.42 to 8.11 fluidounces) of oil raised the pressure in the vena cava, while that in the aorta and pulmonary vein was unchanged. When an additional 10 c.c. (2.71 fluidounces) or more was injected, there was produced a sudden fall in the pressure, both arterial and venous. As soon as the intrapericardial pressure exceeds that in the vena cava, the auricles collapse, and the ventricles, failing to receive a sufficient supply of blood, can no longer maintain a normal pressure in the aorta. If the intrapericardial pressure be maintained, cardiac failure will soon occur, but if a small amount of the fluid be removed, the blood-pressure and circulation are rapidly reëstablished.

In pericarditis, with effusion, the very same thing occurs, except in pericarditis, and the pressure of the effusion is exerted upon the abnormal tissues of the heart and pericardium.

ADHERENT PERICARDIUM

Synonyms.—Adhesive pericarditis, obliterated pericardium, synechiæ pericardii, concretio pericardii cum corde, chronic mediastinopericarditis are all synonymous with adherent pericardium.

Definition.—Adherent pericardium, as the term indicates, is a condition in which the sac is partially or completely obliterated by adhesions. It cannot be considered as a primary clinical entity, as it is always secondary to some previous pericardial disease, usually some form of pericarditis. The clinical symptoms and signs are not due to the obliterated sac alone but result from the associated pathology, the symptom complex of which is sufficient to give it special consideration and by which an adherent pericardium is recognized.

Etiology.—In the greater number of instances, it is secondary to pericardial disease, particularly pericarditis of any form. Every type of infection, or disease, capable of producing inflammatory involvement of the pericardium must be considered as etiologic factors. The most frequent and important are rheumatism, pleuropneumonia, and tuberculosis. In some instances the primary disease is mediastinal, such as mediastinitis, an aneurysm, or malignant involvement. As regards age, it occurs more often in childhood and early adult life, as might be expected, since it follows in the course of pericarditis.

Symptomatology.—Adherent pericarditis presents no characteristic clinical picture. With such a varied possibility in the morbid anatomy, there could scarcely follow any fixed or regular chain of symptoms. For convenience of description, the cases may be subdivided into the following: (1) silent group; (2) those presenting the symptoms of chronic heart disease; and (3) those with Pick's syndrome.

1. When the adhesions are purely intrapericardial, no symptoms are present, the condition is unrecognized clinically and can be determined only by autopsy. The pericardium is so loosely attached, the mobility so great, that partial or complete obliteration produces no symptoms. The only possible exception, as previously mentioned, that may occur, is when the fibrous bands constrict the vessels at the base of the heart. Even this must be extremely infrequent and probably productive of but slight, if any, symptoms.

2. The usual manifestation of adhesive pericarditis are those of a chronic heart disease, not due primarily to the adhesions, but to the associated cardiac pathology. Precordial discomfort, or actual pain, is fairly common and may be due to a subacute inflammation in the sac, in the adjacent pleura, or in the mediastinum. Palpitation, dyspnea, cough and systemic disturbances are the rule.

The most frequent associated cardiac lesion is a myocarditis; this is practically always present. Valvular disease of some form ranks next in order of frequency.

It should be emphasized that the clinical phenomena of adherent pericarditis is in no way characteristic, that the associated cardiac pathology is responsible for the symptoms in the earlier stages, and the effect of the adhesions becomes manifest only when the traction is sufficient to interfere with the compensation. Extensive fixation of the pericardium may occur without clinical symptoms. Temporary disturbance of compensation may follow some physical exertion or prolonged cardiac strain.

3. Pick's syndrome is a recurrent ascites; no edema of the legs, with an enlarged, firm liver, should at once arouse suspicion of pericardial disease and lead to a careful examination.

Physical Signs.—*Inspection.*—As might be inferred from a consideration of the morbid anatomy and clinical symptoms, the intrapericardial type of adhesions produces no physical signs. Clinical and physical phenomena occur only when the obliterated sac is associated with adhesions binding it to the surrounding tissues. When this occurs, various signs may be present, many of which are determined by inspection.

Systolic retraction of the chest wall, particularly in the lower precordial region, is the most important single sign. The retraction may be only slight, limited to one or two interspaces; sometimes the costal cartilages and epigastric region, as well as the interspaces, are decidedly drawn in with each cardiac contraction. Retraction of the interspaces does not possess much diagnostic value, as this is often present in large dilated hearts or in obliterated pleuropericarditis without an adherent pericardium. Even in health this may be observed over the upper precordial area; perhaps it is the expression of marked mobility of the heart and failure of the lung to fill in the space, so it becomes distressed.

In aortic regurgitation, it is common to observe systolic retraction of the lower precordial interspaces, due to atmospheric pressure compensating for the great reduction in the size of the heart and intrathoracic pressure during systole. The same phenomenon may exist in cardiac dilatation from any cause. Adhesions between the pericardium and chest wall due to a pleuropericarditis may produce intercostal retraction, synchronous with the heart's contraction from the cohesion within the normal pericardium. When the ribs, costal cartilages, perhaps lower sternum, as well as the intercostal spaces, are retracted, the significance and conclusion indicates an adherent pericardium.

Skoda called attention to systolic retraction of the apex beat as a sign of importance. Subsequently this was brought into question by Traube, Riegel, Friedreich and others, mainly on the undetermined physiological ground as to the manner of contraction of the heart. Skoda was of the opinion that, during contraction, the heart decreases not only in the transverse diameter but in the longitudinal as well. However this may be, physiologically, in adherent pericarditis with adhesions between the apex and chest wall, a systolic retraction of the apex beat still remains a valuable clinical sign.

Perhaps the next finding in the order of importance is the diaphragm sign of Walter Broadbent. When adhesions exist between the pericardium and diaphragm, the cardiac tug is exerted on the thoracic attachment of the diaphragm, with a visible retraction of the intercostal spaces. This is best observed between the eleventh and twelfth ribs on the left side posterior. Broadbent's sign is usually considered of much clinical value but is not pathognomonic. The same phenomenon may be observed occasionally in large hypertrophied hearts, where no pericardial obliteration is present. Sir William Broadbent has directed attention to the failure of the diaphragm to descend during inspiration, when its activity is restricted by adhesions to the heart.

At least two of the peripheral signs are determined by inspection of the cervical region. Friedreich's sign, a diastolic collapse of the cervical veins, is due to a sudden emptying of the vessels as the right heart rapidly dilates from the traction of the adhesions, following the tension during systolic contraction. The more extensive and firm the adhesions, the more pronounced the diastolic collapse; in some instances it is so complete that the vessel is not only collapsed but the overlying tissues appear depressed.

Kussmaul's sign is an inspiratory swelling of the cervical veins, occurring at the height of inspiration and resulting from mechanical interference with the venous flow from the stretched adhesions about the base of the heart.

Under normal conditions, according to the laws of gravity, the heart will shift from side to side, with change of position of the individual. This is always more marked to the left. With adhesions between the heart and chest wall, the apex on palpation is fixed. Fixation of the apex does not however signify pericardial adhesions, as the cardiac mobility may be limited by a pleural effusion, pulmonary consolidation, neoplasm or some other conditions. Palpation may detect a diastolic rebound at the apex, produced by the cardiac impact from the traction of the adhesions at the beginning of diastole. When present it is probably the most valuable single sign and by many clinicians is considered pathognomonic; but unfortunately it is not a frequent finding.

Percussion.—Percussion usually reveals a much increased cardiac dulness, increased from the associated cardiac pathology and the indurative mediastinopericarditis. Of far greater importance is the absence of the respiratory excursion along the borders of the area of heart dulness, which is fixed and fails to move with respiration or change of position. Some mobility and respiratory excursion may be present, even though adhesions exist. Pulmonary emphysema not infrequently interferes with the determination.

Auscultation.—On auscultation, it is usually possible to detect cardiac murmurs due either to an endocarditis or a myocarditis. In the advanced stages, with cardiac dilatation and a failing heart, a systolic murmur is practically always present. These findings can hardly be considered indicative of pericardial adhesions. Occasionally there may be heard at the apex auscultatory findings of real value. Instead of the coupled first and second tones, three sounds are audible, with the accent on the last. This accentuated sound is synchronous with the palpatory rebound of the apex and possesses the same etiological and clinical significance.

Pulse.—Pulsus paradoxus of Kussmaul, in which the radial pulse during inspiration becomes small and weak, sometimes imperceptible, may be present. While usually described as one of the findings in adhesive pericarditis, it possesses but little diagnostic value either as a sign of adhesions or a pericarditis. Its presence is of relative value when associated with the other physical findings indicative of pericarditis.

Other Physical Signs.—Other physical signs, more or less important, may be present and combined with the findings already described will assist in filling out the clinical picture. For completeness, a few of these should be mentioned. Skoda emphasized a prominence of the precordia as a sign of pericardial adhesions when an effusion could be excluded. Like some of the other findings, this is more valuable as indicating a cardiac hypertrophy. Marked increase of the cardiac impulse, often undulatory in character, beginning at the base, may be observed.

Tuczek and Riegel have described a finding which they consider important as indicating the presence of even limited adhesions. During inspiration, the normal apex beat becomes weaker; during expiration it is stronger. If pericardial adhesions are present, the apex findings are reversed,—stronger during inspiration and weaker during expiration.

Perez's sign consists of a creaking sound on auscultation over the sternum when the patient elevates and lowers the arms, produced, presumably, by the movement and friction of the mediastinal adhesions.

Pick's syndrome, while primarily an adherent pericardium, produces chiefly abdominal and hepatic symptoms, more suggestive of a cirrhosis. The condition is usually described along with the other forms of liver diseases, and for further description the reader is referred to that section.

ROENTGEN EXAMINATION.—By this method no assistance can be had in the simple intrapericardial type. Much information may be obtained by fluoroscopic and plate examination when the obliteration is accompanied by external pericardial adhesions.

Fluoroscopy is particularly important as this will give definite information as to the size and outline of the heart shadow, and will also aid in determining the mobility of the heart and diaphragm. Fixation of the heart and diaphragm by adhesions is, probably, the most important finding, but does not, of course, necessarily indicate an obliterated pericardium. Simply by indirect inference, detecting the associated secondary pathology of adhesive pericarditis, one is justified in concluding that the initial lesion is also present. This becomes more certain or an actual reality when the fluoroscopic findings, the clinical history, and physical signs are correlated. Single or bilateral pleurisy, adhesive or with an effusion, is not infrequently found and may constitute the thoracic changes in a Pick's syndrome. Roentgenograms are also of service but will fail to furnish any additional service, in fact not as much as the fluoroscopic, unless multiple plates be made with the patient in various positions. When this is done, the cardiac fixation as well as pleural or diaphragm adhesions may be determined. Repeated roentgen examination of patients with pericardial effusions, during convalescence, often reveals considerable enlargement of the cardiac shadow. The same finding is frequently observed in adhesive pericarditis, the shadow apparently exceeding the area of dulness on percussion. This discrepancy may occur, due to inability to outline the heart dulness in the presence of an emphysema or perhaps from the accompanying indurative mediastinitis.

Diagnosis.—It would be difficult to select many, if any, diseases presenting a greater range of diagnostic possibilities than may be encountered in adhesive pericarditis. The variations are so great as to be quite sufficient to satisfy the most exacting. From a symptom-complex with an easily determined diagnosis, there are varying degrees of manifestations and diagnostic certainty, even to the vanishing point. The diagnosis may be relatively easy, when there is an accurate history of infection with cardiac symptoms, and when the patient has been under observation and carefully examined, finally developing the clinical picture as already described. Perhaps no single sign is sufficient as a basis for diagnosis, but the symptom-complex is clear and decisive. Mistakes in diagnosis are rather ones of omission than misinterpretation. Too often the possibility of pericardial involvement is entirely ignored. The usual symptoms are those suggestive of cardiac disturbance with associated physical findings and diagnosed as valvular or myocardial disease. If there is a good clinical history obtained from the patient or previous medical attendant, and a careful thorough physical examination is made, there should be no ground for doubt or mistake. There may, however, be mitigating circumstances, some valid reason for excuse, when the patient is examined for the first time, without any obtainable history and perhaps with the heart in broken compensation. At the best, only a tentative diagnosis can then be made.

The differential diagnosis is usually most concerned with aortic regurgitation or with a cardiac dilatation from any cause. The confusing similarity consists in the local cardiac signs, the enlarged area of dulness with the systolic retraction of the intercostal spaces and perhaps slight retraction of the costal cartilages. When in doubt as to an aortic regurgitation, an appeal to the peripheral circulation will at once render a decision possible.

Dilatation of the heart often presents greater difficulty in differentiation, and sometimes constitutes an actual impossibility, particularly when the dilatation is due to a failing heart secondary to an adherent sac. Besides the increased dulness and systolic intercostal retraction, cardiac dilatation is capable of producing Broadbent's sign, the existence of which usually arouses the suspicion of adherent pericarditis. Dilatation of the heart, besides failing to present other evidence of pericardial obliteration, is usually associated with some cardiac, renal, vascular or pulmonary disease.

What has been said in reference to mistakes in diagnosis, applies particularly to the recognition of Pick's syndrome, pericardial pseudocirrhosis. The attention is centered on the liver and abdominal phenomenon to the exclusion or neglect of other possibilities.

Treatment.—MEDICAL.—The therapeutic indications are to prevent the formation of the adhesions and to combat the effect when once produced. Unfortunately, there is no course of procedure that will ensure a return of the pericardium to normal when once involved in a pericarditis. The measures as outlined in the management of the acute stages may be of some service,—how much cannot be stated. Drug therapy is practically of no service; much more may be accomplished by non-medicinal measures. Carefully regulated **exercise** and **diet**, with good **elimination,** are all important. Systemic, graduated exercise may assist in developing and maintaining a compensatory hypertrophy.

When the compensation is no longer adequate, with symptoms and signs of a failing heart, the therapeutic indications are the same as in cardiac disease. Every effort should be made to relieve the heart of the over-load and, at the same time, to support the failing myocardium.

Complete physical and mental rest should be insisted upon; relief of the right heart, by instituting **free catharsis** if the time will permit, should also be insisted upon. When the condition is critical, **venesection** should be done at once. **Digitalis, strophanthus, camphor oil, caffein and strychnia** are some of the remedies which may be of service. Due to the degenerated myocardium, digitalis and strophanthus may have little or no effect. Strychnia is sometimes of greater service.

Surgical.—Adhesive pericarditis produces a fatal termination by mechanical interference with the heart and results in a cardiac dilatation. Medical treatment is helpless to prevent the formation or effect the absorption of the adhesions. Surgery has attempted to supply the demand. Weill of Lyons (1895) and Delorme (1898) have proposed that the adhesions between the visceral and parietal layers be separated. Leriche (1909) suggested that excision of the pericardium be done and considered it preferable to the breaking down or removal of the adhesions. Neither operation has actually been done, and can hardly command serious consideration because of the gravity of the surgical risk and the practical certainty that the adhesions would reform.

A safer and practical procedure, suggested by Brauer and first performed by Peterson and Simon (1902), consists in **resecting two, three or more of the costal cartilages and ribs,** with the **periosteum,** overlying the heart. The object to be attained is the elimination of one of the fixed unyielding points, so that the heart may function unhampered. **Cardiolysis, Brauer's operation,** is the one of choice, as it meets the indications and gives relief, providing the functional integrity of the heart is still maintained.

Prognosis.—The gravity in any individual case depends upon the extent of the adhesions and the ability of the heart to maintain a circulatory equilibrium. The intrapericardial type, with partial or complete agglutination of the sac, unable to produce symptoms or signs, can have no unfavorable influence on the prognosis. Such an individual leads a normal, active life, dies, probably, from some other disease, and the pericardial adhesions are first revealed at autopsy.

With indurative mediastinopericarditis, the immediate outcome depends chiefly upon the following: the cardiac possibilities; whether the myocardium is seriously damaged or not; the degree of mechanical hindrance; and if compensating hypertrophy has occurred. Then, too, much will depend upon the kind of life the patient can follow. The laborer, who must work at physical toil, even before he is able, who disregards his physical condition, must present a prognosis far more unfavorable than the individual with means, who can seek advice and live a life of ease and comfort. The ultimate prognosis is relatively bad, depending upon the progressive or stationary character of the lesion. Usually, sooner or later, the hypertrophy is inefficient, cardiac dilatation occurs, and the usual symptoms and signs of cardiac failure appear. Such an event is always grave and a fatal termination not far distant. Weakness and disappearance of the apex and precordial retraction is always an unfavorable sign, indicating increasing heart weakness.

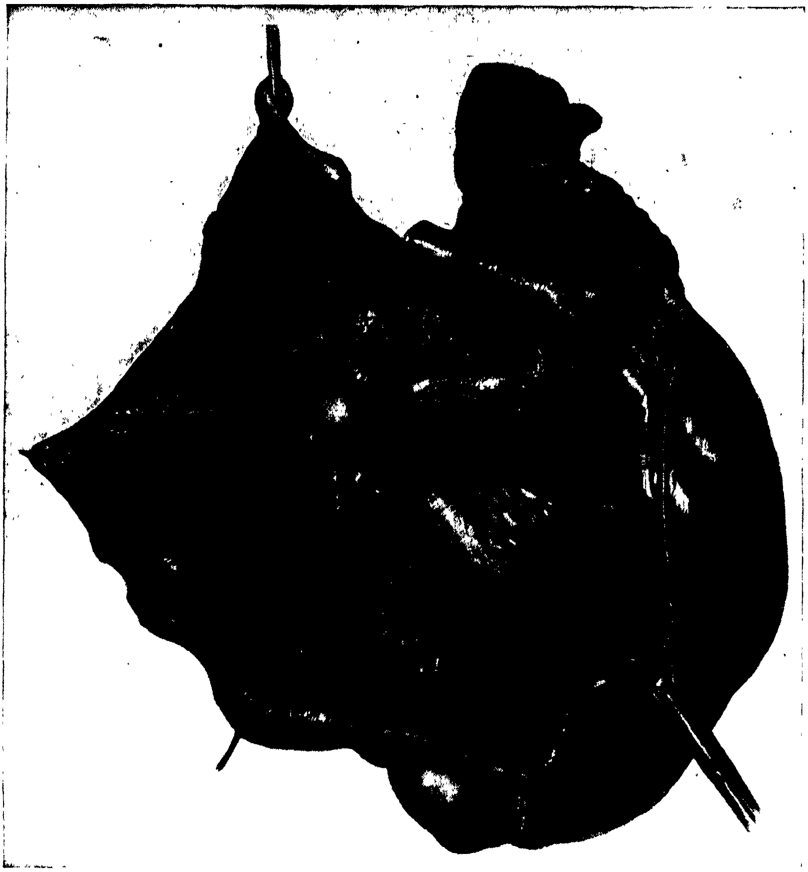


FIG. 5. ACUTE FIBRINOUS PERICARDITIS. THE PERICARDIUM HAS BEEN REFLECTED AND REVEALS THE FIBRINOUS EXUDATE AND SUBSEROUS HEMORRHAGES.

Rheumatic mediastinopericarditis in early life is relatively far more serious, due to the usual accompanying endomyocarditis and the tendency to recurrence. Death usually occurs from gradual cardiac failure, with the heart in asystole; sometimes the termination is sudden and abrupt.

Morbid Anatomy.—The etiology and anatomical changes are so varied that it is possible to group the cases according to the predominating findings, which may be entirely limited to the sac, and accompanied by adjacent mediastinal and pleural pathology, by cardiac disease, or even by changes in the liver.

Pericardial Lesions.—As previously mentioned, under acute pericarditis, a dry plastic exudate, when limited in amount and extent, may entirely disappear and the pericardium may return to normal. Generally, perhaps with very few exceptions, the fibrinous exudate becomes organized and the pericardial layers adherent. This may be partial or complete, so that no part of the pericardial sac remains.

When partial, the adhesions may occur only at the base of the heart, perhaps posteriorly or anteriorly; sometimes they occur laterally, but rarely in the apical region. In extensive or complete involvement, the fibrous formation is always more marked on the cardiac side. When the exudate is serofibrinous or hemorrhagic, the fluid is absorbed and the same ultimate results are produced, except that simple or multiple loculation of the fluid may occur.

The purulent and tuberculous types may produce not only adhesions but go on to a cartilaginous-like or calcareous formation. The author can recall one case of an elderly man who was admitted to the hospital in a dying condition. No history could be obtained, but the clinical symptoms were those of a decompensated heart. The autopsy revealed an enormous, thickened, calcified pericardium; in fact, the heart was partially enclosed in a shell-like bag. More frequently the calcification is limited and circumscribed to certain areas.

Mediastinal and Neighboring Tissue Lesions.—Adhesions may form and bind the pericardium to the anterior chest wall; they are usually secondary to the pericarditis. More frequently, there is an accompanying mediastinitis, which results in a fibrinous formation, fixing the obliterated pericardium to the anterior chest wall, to the spine or to the great vessels and the esophagus behind. The same process often produces adhesions between pericardium, pleura and thoracic wall as well as the diaphragm. It is chiefly upon the occurrence of this mediastinopleurisy that the clinical manifestations and recognition of adherent pericarditis really depends. In the order of sequence, the pleuromediastinitis is usually secondary but it may be primary.

Cardiac Lesions.—The heart is practically always involved in pericarditis either as a result of the same infection that produces the pericarditis or of the mechanical disturbance due to the adhesions. Simple adherent pericarditis, when the adhesions are limited to the sac in the presence of a normal endomyocardium, produces no anatomical changes in the heart. The pericardium possesses such a range of freedom that partial, or even complete obliteration, can have no injurious effect. A possible exception may occur where the adhesions are most marked about the base, and when they are particularly strong and constrict the vessels, especially the vena cava.

If the adhesive pericardium is accompanied by adhesions due to a pleuromediastinitis, or to an endomyocarditis, the heart invariably presents changes, either because of the infection or because the condition is secondary to the mechanical difficulty. Both a dilatation with hypertrophy and an atrophy of the heart have been described. Undoubtedly the former is more frequent, as the infection is prone to produce an acute endomyocarditis, while the acute pericarditis is accompanied by a limited or extensive myocarditis. Both conditions weaken the heart with a resulting dilatation, long before the sac becomes adherent. When adhesions form, the work of the heart is increased, which results in more dilatation or in a gradual compensatory hypertrophy.

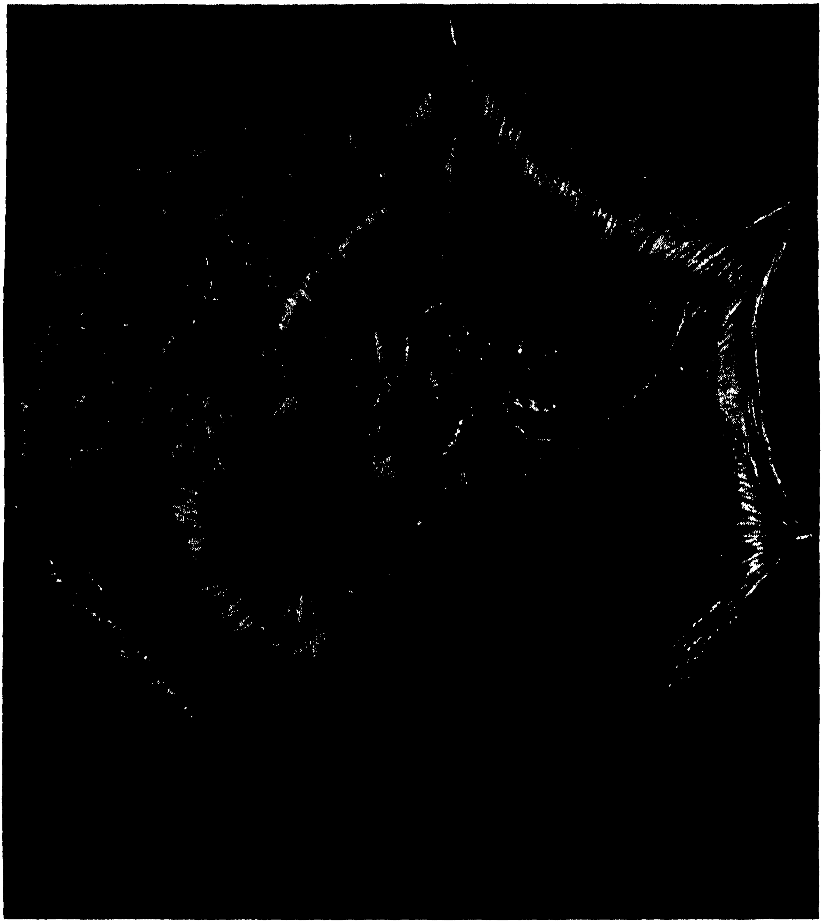


FIG. 6. ACUTE SEROFIBRINOUS PERICARDITIS. INCISED PERICARDIUM, ONLY PARTIALLY REFLECTED, DUE TO THE ADHESIONS AND BANDS OF ORGANIZED FIBRIN.

HEPATIC LESIONS.—It sometimes happens that the changes secondary to the obliterated pericardium become pronounced and dominate the clinical picture. This is particularly true in the hepatic disturbances, closely simulating a cirrhosis, which has come to be known as Pick's syndrome, or pericardial pseudocirrhosis, first described by Friedel Pick in 1896. Since then much has been written on the subject, especially by Rolleston and Kelly. Due to circulatory disturbances, the liver becomes extremely engorged with what is finally a fibrous hyperplasia. Limited perihepatitis, with peritoneal adhesions, is frequent, but this condition was considered by Pick as accidental and not an essential part of the process.

Sometimes the adherent pericardium and perihepatitis are associated with a unilateral or bilateral pleurisy and peritonitis—a multiple serositis or polyserositis. Kelly has grouped together, under the term multiple serositis, the cases presenting the findings of a Pick's pericardial pseudocirrhosis and the "iced liver" or "Zuckergussleber" of Curschmann. Pick's syndrome is characterized by the presence of recurrent ascites, no edema of the legs, an enlarged, firm liver, and the symptoms and signs of adherent pericarditis.

Pathological Physiology.—Adhesive pericarditis may mechanically interfere with the cardiac function by either increasing the work of the heart or by constricting the vessels at the base of the heart. What effect the adhesions may have, will be greatly determined by their location, length and density, and by the fact as to whether they are limited or extensive. Adhesions, limited to the sac, will have no appreciable effect on the heart or circulation. When the adherent pericardium is bound by adhesions to the chest wall, diaphragm and surrounding structures, changes in the heart and functional disturbances occur. Antedating the period of adhesion formation, the heart is usually more or less dilated, due to the myocarditis, accompanying or secondary to the pericarditis, which may be manifest by symptoms and signs. Since the period of organization of the fibrin and the formation of adhesions is relatively slow, the work of the heart is gradually increased. This results in added physiological activity which produces a compensating hypertrophy, providing the myocardium is not seriously damaged.

If the myocardium is in a condition unable to respond to the additional demands, no hypertrophy will occur; the heart is only more embarrassed and the circulatory disturbance more pronounced. While the adhesions, up to a certain point, may be advantageous and desirable, this is soon overbalanced by the harm and danger of cardiac dilatation, as the mechanical interference exceeds the physiological possibilities of the heart. The traction of the firm, unyielding adhesions interferes with cardiac systole and increases the diastole, which finally results in heart failure. The clinical symptoms will be determined by the location of the adhesions, and upon which part of the heart the traction is most pronounced. If the traction is exerted on the left ventricle, the symptoms indicate pulmonary involvement, such as dyspnea, cardiac asthma, pulmonary engorgement, or edema. With traction on the right heart, the disturbances are those of a systemic venous stasis, such as tricuspid insufficiency, and all the usual and familiar manifestations of a broken compensation. When the adhesions are extensive, with traction on both the right and left heart, the pulmonary and systemic disturbances will coexist. As the adhesions become more abundant and more dense, the heart is subjected to increased traction, and dilatation is the inevitable result. The compensatory hypertrophy is no longer able to keep pace with the growing demands and heart-failure occurs.

HYDROPERICARDIUM

Definition.—Hydropericardium or hydrops pericardii is a condition in which there is an increased amount of serous fluid in the sac; it is non-inflammatory in type. It can hardly be considered as a separate pathological or clinical entity, occurring only as a result of some other process and not as a disease. Much uncertainty exists in attempting to give a satisfactory definition, when indicating what is to be considered an abnormal amount of the pericardial fluid. Ordinarily the sac contains only just a sufficient amount to moisten the layers, but a small amount could hardly be considered as exceeding the physiological limit. Autopsy reveals usually from 5 to 20 c.c. (1.35 to 5.42 fluiddrams), or even 100 c.c. (3.38 fluidounces), but this cannot be considered normal, as the pericardial fluid increases at the time of death. Hydropericardium is analogous to hydrothorax and ascites; the fluid is a transudate, clear, light straw-colored; it has a low specific gravity, an alkaline reaction, low cell and albumin content, various salts, urea and occasionally sugar. Clinically hydropericardium is a rare condition when compared with hydrothorax and ascites, although it is frequently found at autopsy.

Etiology.—Hydropericardium occurs only as a secondary process in the course of some disease, producing a disturbance of the pericardial circulation, and increasing the amount of transudate beyond the normal limit. The primary lesion may be local or general. The local diseases include the various valvular and myocardial lesions, coronary sclerosis, thrombosis of the cardiac veins, diseases of the lungs, as emphysema, pulmonary fibrosis and any other conditions associated with increased intracardiac pressure in the right auricle or in the coronary veins. Mediastinal tumors, aortic aneurysm and pericardial tubercle by mechanical pressure can produce the same effect.

The general causes include the diseases accompanied by a cachexia or secondary blood changes, as carcinoma, tuberculosis, and nephritis. Any disease associated with a dropsy may be etiologically responsible for a hydropericardium; this means that the primary lesion may be cardiac, pulmonary, renal or general. When a transudate occurs in the various serous cavities, as in a general dropsy, the pericardium is usually involved, but the pericardial accumulation is late in its development.

Symptomatology.—Hydropericardium produces no symptoms, except when the amount of the transudate is excessive and mechanically interferes with the cardiac and pulmonary function. The symptoms present are those of the disease producing the increased transudate, whatever that may be. The fluid may accumulate slowly and reach a considerable amount without arousing any suspicion of its existence, being entirely masked by the manifestations of the disease upon which it depends. When symptoms are present, the manifestations are the same as those which occur in a pericarditis with an effusion but without the inflammatory phenomenon.

Physical Signs.—The findings on physical examination will depend upon the primary disease and the amount of the transudate. Generally speaking, the findings are identical with those of pericardial effusion minus the ones due to infection. Pain, fever and a friction rub are absent. In hydropericardium, the apex beat is often easily palpable and the cardiac tones good and loud, as the myocardium is less frequently involved.

Diagnosis.—The clinical recognition of hydropericardium will depend upon the physical signs of a pericardial effusion from which it must be differentiated. This may be done by a careful consideration of the history, the development of the disease, and the physical signs. Clinical manifestations of fluid in the pericardium, without a history or symptoms of an infection, associated with findings of fluid in other serous cavities, are strong eivdence in favor of hydropericardium. Owing to the character of the primary disease, or to the limited amount of the fluid, and particularly as it occurs as a terminal process, the diagnosis is often overlooked. Oftentimes the diagnosis at best is but tentative and an absolute determination will depend upon a pericardial puncture. In one instance of mediastinal neoplasm with a large cardiac dulness, it was impossible to demonstrate or exclude a hydropericardium except by puncture, which revealed, on two occasions, a characteristic transudate.

Treatment.—Therapeutic efforts should be directed to relieve or minimize the primary disease. The treatment for a failing heart, pulmonary or renal disease, of which the hydropericardium is only a part, demands first attention. **Aspiration** will be necessary when the distention is pronounced and may require repeating. The relief afforded oftentimes is pronounced, but can be only temporary, as the fluid quickly reaccumulates; this, of course, depends upon the primary disease.

Prognosis.—The primary causative disease is the determining factor, not the hydropericardium, except when it reaches an unusual size and produces mechanical difficulty. Occurring usually as a terminal event, its presence indicates only a downward course and an unfavorable outcome.

HEMOPERICARDIUM

Definition.—As the term indicates, hemopericardium is an accumulation of blood in the pericardium. It is not to be confused with the hemorrhagic effusion encountered in a pericarditis or associated with a malignancy, tuberculosis or scurvy. Alcoholism and phosphorus poisoning may cause a hemorrhagic effusion into the pericardium, but it does not constitute a real hemopericardium.

Etiology.—The causes of hemopericardium may be surgical or medical. The surgical group includes injuries to the pericardium and its contents, injuries due to a stab or to gunshot wounds, and crushing injuries to the chest. Thoracic surgical operations, pulmonary or cardiac, may be a possible cause. Paracentesis of the pericardium or the heart for therapeutic purposes has been followed by a hemorrhage into the sac. The medical group includes such causes as spontaneous rupture of the heart, rupture of an aortic aneurysm or of a sclerotic coronary artery. In the order of frequency, ruptured heart stands first. When the heart ruptures, there is usually a myocardial degeneration which occurs during violent physical exertion. Less frequently the hemorrhage may be due to a cardiac aneurysm, a suppurative myocarditis with localized abscess formation, or to any condition producing a weakness of the cardiac walls, particularly when accompanied by an increase of the intracardiac pressure. When an aortic aneurysm is the cause, it is usually small and intrapericardial, but it may be located in the ascending arch, and, by dissecting downward, rupture into the pericardium. Rupture of a caseating or suppurating tuberculous tracheobronchial or mediastinal gland is a possible but rare cause, as reported by Eichorst.

Symptoms and Signs.—The symptoms are variable, depending as they do upon the amount and rapidity of the hemorrhage. If the rupture is large, with a rapid escape of blood, producing sudden distention of the sac, the symptoms of cardiac distress and heart-failure will be present with a fatal termination within a few minutes or hours. The general condition of the patient may suggest that of surgical collapse. Physical signs of the hemorrhage, so far as the pericardium is concerned, are usually wanting. Most frequently the termination is so sudden that no opportunity is afforded for physical examination. When the course is less rapid, the symptoms are those of cardiac disturbance and an internal hemorrhage. The patient may experience a sensation as if something had given away in the region of the heart; perhaps anginoid pains may be present with vertigo, syncope or convulsive seizures. Pallor, weakness, a small or imperceptible pulse may also be present. With these symptoms, the gradually distending sac presents the physical signs of an effusion, similar to those of a pericarditis with effusion or a hydropericardium. Symptoms and signs of the primary disease may also be present.

Diagnosis.—In the acute cases, the diagnosis is made usually at autopsy. The cause of sudden death may be suspected, if the patient has been under observation with some one of the diseases enumerated in the etiology. If there is a history or evidence on examination of some injury, as a stab or gunshot wound, with symptoms and signs of hemorrhage and a distended pericardial sac, a reasonable diagnosis will be possible. Obtaining blood on exploratory puncture will definitely determine the diagnosis.

Treatment.—Medical or surgical treatment in the acute cases is only a little short of useless, as it is impossible to remove or correct the cause. In the slowly developing form, the medical indications consist of **symptomatic relief** and employing such means as may increase the **coagulability of the blood.** Single or repeated **aspiration of the blood** has resulted in recovery. The surgical causes may present far better chances of controlling the hemorrhage by operation, either **ligation** or **suturing,** as the condition may demand.

Prognosis.—The prognosis is always grave; the ones due to ruptured heart or aneurysm are practically always fatal in a very short time.

Penetrating and crushing injuries with a small hemorrhage may be brought to recovery.

Morbid Anatomy.—This includes the underlying primary process and the presence of blood in the pericardium. The amount of blood will depend upon the size of the rupture and the rapidity of the escape. The blood may be fluid or coagulated. When the escape is rapid, the amount is small and soon fatal. If the accumulation is slow, the sac is gradually distended; the amount of blood may be considerable and coagulated or deposited in layers, due to recurring hemorrhages.

PNEUMOPERICARDIUM

Definition.—Pneumopericardium is a collection of air or gas in the pericardium. Analogous to a similar process in the pleura, there may be a pure pneumopericardium, but usually it is combined with an effusion constituting a hydropneumopericardium, with pus, with a pyopneumopericardium, or with blood—a hemopericardium.

While accurately described and recognized by the older authors, it can be regarded only as a rare occurrence. W. B. James, in 1904, in a careful review of the literature, was able to find but 37 undoubted cases; with his own this made a total of 38. Cowan, Harrington and Riddell, in 1913, increased this number by 6 additional cases, 5 in the literature and their own case reported. Since that time a careful search of the literature reveals but 3 additional recorded cases, 2 of which were artificially produced for therapeutic purposes.

Etiology.—Air or gas may collect in the pericardium whenever there is established a communication between the sac and the external atmospheric air, or whenever gas is generated in the sac by a gas-producing organism or by putrefaction.

One group of causes includes penetrating wounds of the pericardium due to stab, gunshot wounds, and injuries of the chest, such as fracture of the ribs with injury to the lung and pleura, surgical operations and entrance of air during exploratory puncture or aspiration of the pericardium. This group constitutes a fairly large proportion, 12 of the recorded cases, 10 of which followed puncture of the pericardium.

A second group includes the causes producing a communication with an air-containing viscus, either thoracic or abdominal. Perforations of the esophagus by simple or carcinomatous ulcer or by injury with a foreign body, as in sword-swallowing, have been reported. In 5 cases the esophagus was perforated, in 3 by carcinomatous ulceration. Among the thoracic diseases, tracheobronchial adenitis, emphysema, pneumothorax, pneumonia and gangrene have been described. In 4 cases a caseating tuberculous focus in a gland, or in the lung, established a communication between the sac and bronchus or esophagus. Air or gas may enter the sac through a communication with the abdominal organs, such as the stomach or intestines; there were 2 cases on record. Peptic ulcer, gastric or duodenal and gastric carcinoma with ulceration are the most frequent causes. Hepatic abscess as well as appendiceal abscess have been found as a possible cause.

A third group comprises those cases in which no opening into the pericardium can be found, and in which an infection of the sac exists and becomes distended by gas from a gas-producing organism or from putrefaction. Undoubtedly some of the cases reported by the older writers were due to gas formation or to putrefaction, and very likely they were postmortem changes. Although no specific form of organism has been described, from analogy it is reasonable to conclude that the *Bacillus aerogenes capsulatus Welcheii* is probably the exciting cause, as is true in the case reported by Nicholls. Practically any form of infection producing a purulent exudate may undergo putrefaction and gas formation.

The fourth group is composed of the cases of pericarditis in which air or gas is intentionally introduced for therapeutic purposes; this operation produces an artificial pneumopericardium such as is described by Weil and Loisceleur.

Symptoms and Physical Signs.—All symptoms may be wanting, especially when the condition develops slowly, or when the manifestations are those of pericarditis; this is particularly true of the pressure symptoms, as the sac becomes distended and interferes with the pulmonary and cardiac function. When the air or gas enters rapidly as in perforating wounds, the patient complains of precordial discomfort, pain, dyspnea, weakness and perhaps attacks of syncope. Symptoms and signs of cardiac failure and shock may be present.

The physical findings are characteristic, in most instances permitting a clinical diagnosis as evidenced by the few cases reported by autopsy and overlooked during life. In any doubtful or questionable case, the roentgen examination will be definite and conclusive.

Auscultation.—The most characteristic finding is by auscultation, and consists of the presence of a splashing, churning sound over the precordial area; this is due to the presence of fluid and air, or gas, in the pericardium. These sounds are extremely variable in time and quality but quite synchronous with the heart's action. A metallic tinkling is often heard, superadded to the splashing sound, sometimes heard by the patient and audible for some distance from the patient. The splashing sound has been described by various writers as the "mill-wheel" murmur, the bruit de moulin, and a metallic gurgling. As the fluid increases, the characteristic sounds decrease and may disappear, and the cardiac sounds become distant and muffled.

Percussion.—On percussion, with the patient recumbent in the dorsal position, tympany is present over the cardiac area; with the patient sitting upright, there is tympany over the upper and dulness over the lower portion of the pericardium. Change of position may produce a change in the percussion findings. Occasionally dulness over the air- or gas-filled sac is found instead of tympany, due to the degree of tension present. Cracked-pot sound has also been described, where only a hydropneumopericardium was found without a bronchial communication. The cardiac impulse may be palpable only in the recumbent position; absent or doubtful in the upright. Findings of the associated cardiac and pericardial pathology, as well as the primary disease, may also be determined.

Roentgen Examination.—Confirmatory and conclusive evidence is furnished by roentgen examination. Usually this examination leaves no room for doubt in the presence of the characteristic physical signs, but, if it is not a part of the regular routine examination and any doubt does exist, the patient should be subjected to such an examination.

The fluoroscopic findings and skiagrams are both most characteristic, showing the presence of air or gas in the distended sac. A fluid level, shifting with the position of the patient or with cardiac action, can easily be demonstrated when the pneumopericardium is associated with effusion or exudate into the sac.

Diagnosis.—With the typical physical signs and particularly with a roentgen examination, the diagnosis is easy. There is hardly any other condition which simulates pneumopericardium or produces any confusion. It is conceivable that a pulmonary cavity situated near the heart or perhaps a left-sided pneumothorax might cause some difficulty. Suspension of the abnormal metallic sounds with suspension of breathing, the displacement of the heart to the right, along with palpable cardiac impulse and audible heart sounds, will assist in diagnosis. Roentgen examination will remove all doubts and determine the diagnosis. Traumatic emphysema with air in the pericordial area may be confusing and cause a slight suggestion of pneumopericardium. The stomach distended by gas sometimes is associated with a metallic sound, but differentiation is made possible by careful cardiac examination or by aspiration of the stomach contents.

Treatment.—This must depend chiefly upon the cause as well as the form of the pneumopericardium. If produced by a penetrating external wound, the **opening** should be **closed** and **treated surgically.** In the event of a pericarditis developing, the same measures are indicated as outlined in the treatment of that disease. When it is due to an internal penetrating wound or fistulous tract, the treatment is purely **symptomatic** and **palliative.**

Accidental and unintentional entrance of air into the pericardium during puncture or aspiration should cause little anxiety, as the air is usually rapidly absorbed. Therapeutically it may be of assistance in the treatment of the disease for which the puncture or aspiration was made.

Prognosis.—Pneumopericardium, with its varied etiology, presents a prognosis based mainly upon the primary disease, many of which cases are fatal. When due to the accidental entrance of air during puncture or aspiration of the pericardium, the prognosis is usually favorable, depending upon the type of pericardial involvement.

Morbid Anatomy.—The anatomical changes consist of air or gas in the pericardium with the associated pathology. Pure pneumopericardium is extremely rare; most frequently a pericarditis is present with a serous or purulent, and occasionally, hemorrhagic exudate.

The air or gas occupies the upper portion of the sac, with the fluid in the dependent part. The composition of the air or gas will vary according to the etiology. It may be identical with atmospheric air when the communication is external or similar to that found in the lungs, stomach or intestines, depending upon the location of the perforation. In the closed cases, the gas is usually fetid and foul-smelling. Puncture of the pericardium will allow the air or gas to escape with, sometimes, a distinct sound.

NEOPLASMS OF THE PERICARDIUM

The pericardium may become involved with a malignant or benign neoplasm, which may be primary or secondary.

Malignant Neoplasms.—Either carcinoma or sarcoma may occur.

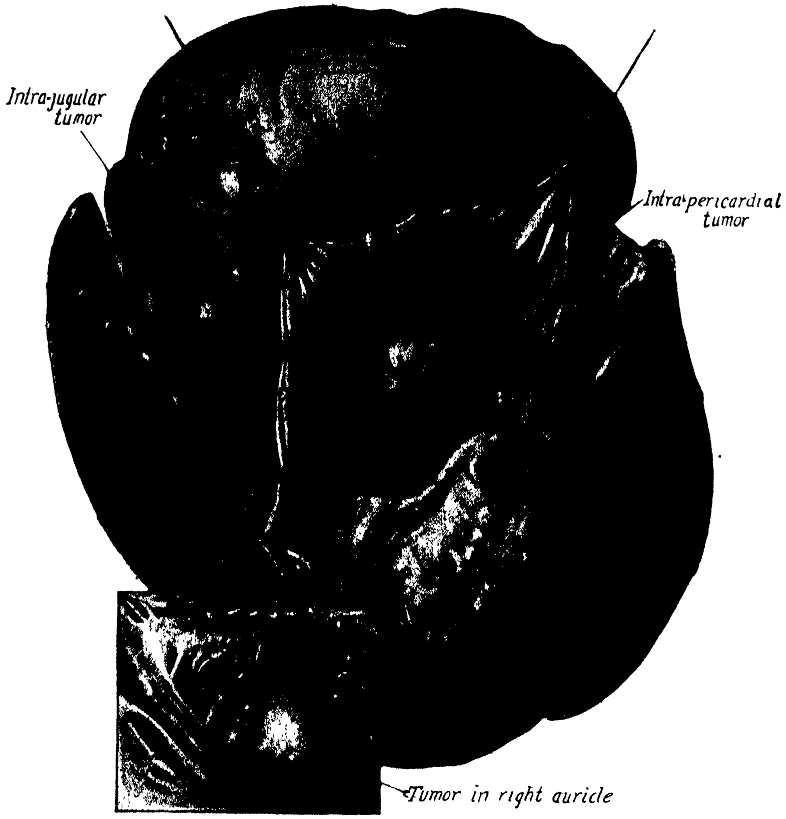


FIG. 7. ANTERIOR VIEW OF LYMPHOSARCOMA, WITH LARGE MEDIASTINAL NEOPLASM, ALSO SHOWING GROWTH INTO PERICARDIUM, RIGHT AURICLE AND RIGHT JUGULAR VEIN. (Courtesy W. B. Saunders Co.)

Primary involvement with either form of malignancy is extremely rare. Primary carcinoma is even denied or seriously questioned but as a possibility it must be admitted. Foster and Guarnieri have reported primary pericardial carcinoma. Broadbent, Redtenbacher, and Williams and Miller have reported primary sarcomas.

Secondary malignancy, while more frequent, is also relatively rare, occurring but six times in 9118 autopsies according to Kobler. Either carcinoma or sarcoma may occur, but the former is more frequent. Usually the primary growth is located in the chest and involves the pericardium by direct extension or by metastases. Mediastinal, bronchial, esophageal, cardiac, pulmonary or pleural malignancy is responsible for the greater number. Malignancy of distant organs, with metastatic secondary growths, may also occur. The secondary neoplasms present the same appearance characteristic of the primary growth. The secondary pericardial growths may be single or multiple, with or without an associated hydropericardium or pericarditis. Located at the base of the heart and with pressure on the coronary circulation, a pericardial transudate can occur. Usually there is more or less pericarditis with a hemorrhagic exudate. Occasionally a purulent or putrid exudate is present, probably due to secondary infection.

Symptoms and Physical Signs.—The symptoms are those of the primary growths associated with the acute or subacute manifestations of a pericarditis. Physical findings will vary according to the anatomical changes; in some the findings will be entirely negative, while in others they will be those of a pericarditis with effusion or of a hydropericardium. Evidence of a primary growth, as a mediastinal tumor, regional adenopathy, or enlargement of the cervical glands, will be of considerable assistance in the diagnosis.

Roentgen examination is indispensable and should always be employed. When the findings indicate fluid in the sac, exploratory puncture or aspiration, when indicated, will furnish valuable diagnostic information. Usually the fluid will be found to be bloody, but it may be clear, purulent or putrid.

Diagnosis.—The recognition of pericardial malignancy depends upon the determination of a primary malignancy, associated with pericardial symptoms or signs of a pericarditis. Without these conditions the diagnosis may be impossible.

Treatment.—The treatment is purely **palliative** and consists in rendering relative comfort. **Opiates** are frequently required to relieve pain or to produce rest. **Repeated aspiration of the sac** may be necessary, or, perhaps, the establishment of **permanent drainage.**

Prognosis.—The prognosis is necessarily bad and the duration usually brief, as the pericardial complication is indicative of extensive involvement.

Benign Neoplasms.—Nonmalignant neoplasms have been reported, chiefly as autopsy findings. Clinically they present little or no interest as their recognition is practically impossible. The reports include fibroid tumors, lymphomas, one case of cystic enchondroma, polypi, and cardioliths. Free bodies in the pericardium, probably from detached polypi, a mass of fibrin or coagulated blood, have also been described.

History.—Pericardial lesions were first recognized and described by Galen from the anatomical investigations and dissections in the lower animals. Senac, by his dissections in man, advanced the knowledge on pericardial diseases but only from the anatomical standpoint. The same may be said of Viensseus, who first described pericardial adhesions, and Griesinger, in his description of mediastinopericarditis. Morgagni made the first attempt to correlate his pathological findings with the clinical symptoms. With the discovery of immediate percussion, Auenbrugger applied his method to the clinical recognition of pericardial disease, which was finally enthusiastically adopted and employed by Corvisart. To Laennec is due the honor of first detecting the pericardial friction rub by auscultation, which he believed at first was due to a pericarditis, but later, unfortunately, this view was discarded. Equal or greater honor is due Collin for first accurately and positively associating the rub with a pericarditis. Among the long list of clinical investigators, the name of Skoda stands preëminent, due to his acute and accurate interpretation of the physical signs of pericarditis.

With the possibility of the recognition of pericarditis, attention was directed to its association with other diseases, especially rheumatism as emphasized by Pitcairn, Dundas, Sibson, Wells and Latham. Bacteriology, by demonstrating the essential causative factors, has furnished an important chapter in the knowledge of this disease.

Riolan proposed tapping the pericardium, but Romero was the first to actually perform pericardicentesis. Schuh and Skoda placed pericardial puncture and aspiration on a safe clinical basis. The latest noteworthy addition to our knowledge in pericardial diseases is due to the application of the roentgen rays.

BIBLIOGRAPHY

General

Achard, C. et Rouillard, J. Deux cas d'endocardite maligne áforme lente. Bull. et mém. de la Soc. méd. d. hôp. d. Par., 1920, xliv, 3rd Series, 1163.

Babcock. Diseases of the heart and arterial system. D. Appleton & Co., N. Y., 1903.

Bopp, W. F. Heart disease in children; segregation of school children with heart disease. Arch. Pediat., Feb., 1921, xxxviii, 86.

Brachman, D. S. Auricular fibrillation; some observations and deductions from a series of 400 cases. Lancet, Feb. 19, 1921, 1, 374.

Broadbent, Sir W. Sarcoma of pericardium. Transactions of the Pathological Society of London, 1882, xxxiii, 78.

Chatard, J. A. Acute pericarditis complicating acute lobar penumonia. Johns Hopkins Hosp. Bull., Balt., 1905, xvi, 334.

Chatin, P. De la péricardite brightique; étude pathogenique. Rev. de méd., Par., 1900, xx, 445–467.

Chauffard. Le frottement péricardique dorsal dans les péricardites brightiques a grand épanchement. Bull. Acad. de méd., Paris, 1916, lxxv, 3rd Series, 23; also Pres. méd., 1916, xxiv, 9.

Chavigny, P. Péricardite avec épanchement pouls paradoxal; valeur de ce signe. Paris méd., 1917, xix, 219–221.

Cholet, R. Gros abcès du myocarde chez le bœuf. Rec. de méd. vet., Par., 1920, xcvi, 42–44.

Christian, H. A. The frequency of pulmonary compression signs in acute fibrinous pericarditis. J.A.M.A., Chicago, 1918, lxxi, 419–422.

Cleland, J. B., and Palmer, A. Case of malignant (carcinomatous) pericarditis. M.J. of Australia, 1920, 1, 233.

Cowan. Diseases of Heart. Lea and Febiger, Phila., 1914.

Denecke, G. Die Bedeutung des Perikards für den Mechanismus der Herzbewegung und deren spezielle Storung bei Perikarditis obliterans. Med. Klinik., 1920, xvi, 657.

Dieulafoy. On subcutaneous pneumatic aspiration as a method of diagnosis and treatment. J. Weiss & Sons, 1877.

Flint, A. Diagnosis, pathology and treatment of diseases of the heart. Phil., 1870, Ed. 2.

Florcken, H. Perikarditis nach Lungenschussen. Deutsche med. Wchnschr., Leipz. u. Berl., 1916, xliii, 979.

Friedlander, G. Zur Frage der Heilbarkeit von Herzklappen fehlern. Deutsche med. Wchnschr., Leipz. u. Berl., 1920, xlvi, 1191.

Gibson. Diseases of the heart and aorta, 1898, p. 381.

Gordon, W. Practical gains of clinical cardiology since 1900. Brit. M.J., Jan. 1, 1921, 1, 12.

Gorham, L. W. Significance of transient localized, pericardial friction in coronary thrombosis (pericardial epistonacardia); report of 6 cases. Albany M. Ann., 1910, xli, 109.

Hall, A. J., and Wilson, J. B. F. A case of traumatic pericarditis due to a needle. Lancet, London, 1917, ii, 856.

Halsey, R. H. Heart disease in children; psychology of the cardiac and the doctor. Arch. Pediat., Feb., 1921, xxxviii, 82.

Hanswirth, L. A case of large pericardial effusion. Med. Rec., N. Y., 1918, lxxi, 419–422.

Hift, R., and Brull, L. Über eine endemisch auftretende hämorrhagische Erkrankung des Herzbeutels. Wien. klin. Wchnschr., 1917, xxx, 357–362.

Heitler, M. Drei Fälle von relativer Insuffizienz der Aortaklappen, die Insuffizienz in einem Falle vorübergehend, in zwei Fallen persistierend. Wien. med. Wchnschr., 1920, lxx, 1249–1253.

Hirschfelder, A. D. Diseases of the heart and aorta. J.B. Lippincott, 3rd Ed., Phil.

Hudek, D. F. Report of a case of pericarditis with effusion. Wisconsin M.J., 1916–17, xv, 53.

Kuno, Y. The mechanical influence of fluid in the pericardium on the function of the heart. J. Physiol., London, 1917, li, 221–234.

Ledford, H. P. Endocarditis in children; analysis of 250 ward cases of acute endocarditis in children. Am. J. Dis. Child., Feb., 1921, xxi, 139.

Lereboullet, P. La ponction epigastrique de Marfan dans la péricardite rheumatismale avec épanchement. Paris méd., 1916–17, xxi, 14.

Levine, S. A. Clinical recognition of various types of paroxysmal rapid heart action. Boston M. and S.J., Jan. 20, 1921, clxxxiv, 53.

Locke, E. A. The occurrence and diagnosis of pericarditis. Boston M. & S.J., 1916, clxxv, 590.

Lutembacher, R. Anevrismes du ventricule gauche. Arch. d. mal. du cœur, etc., Par., 1920, xiii, 49–58.

McPhedran, A. Diseases of the pericardium. Mod. Med. (Osler & McCrae), 2nd Ed., Philadelphia and New York, 1915, iv, 41–77.

Müller, E. F. Perikardtische Verkalkungen. Dis. Greifswald, 1918.

——— Perikarditische Verkalkungen. Fortschr. a.d. Geb. d. Röntgenstrahlen, Hamb., 1918, xxv, 231–243.

Musser, J. H., Jr. Pericarditis and endocarditis. Jr. M. Clinics N. America, 1920, iii, 1403.

Nice, C. M., and Vance, J. G. Etiological classification of heart diseases. Med. Rec., N. Y., 1920, xcviii, 605.

Paetsch, B. Pericarditis exsudativa im Röntgenbilde. Deutsch. med. Wchnschr., 1920, xlvi, 16.

Paterson, D. H. Two cases of congenital heart disease. Proc. Roy. Soc. Med., Lond., 1919–20, xiii, 138–140.

Perera, A. Su due casi di insufficienza aortica. Gazz. med. Napolit., 1920, iii, 137–139.

Peters, J. W., Jr., and Barr, D. P. Disorders of the respiratory function in cardiac disease. Med. Rec., N. Y., 1920, xcviii, 669.

Pezzi, C. Quelques signes peripheriques dans la symphyse cardiaque. La pones de Griesinger-Kussmaul. Arch. d. mal. du cœur. etc., Par., 1918, xi, 201–214.

Picard, H. Die Bedeutung des Perikards für den Mechanismus der Herzbewegung und die spezielle Störung bei Pericarditis obliterans. Med. Klinik, 1920, xvi, 234.

Rhodes, G. B. Suppurative pericarditis. Ann. Surg., 1915, lxii, 660.

Roberts, F. T. Diseases of the pericardium. System of Medicine by Albutt and Rolleston, London, 1909, VI, 26–104.

Robey, W. H. Pericarditis; leading points in diagnosis, treatment and management. Med. Clin. N. Am., 1920, iii, 887.

Romberg, E. Lehrbuch der Krankheiten des Herzens und der Blutgefässe. Stuttgart, 1906.

Rothfuchs. Herzbeutelschuss. Deutsche med. Wchnschr., Leipz. u. Berl., 1916, xlii, 525.

Rubino, A. Les pericarditis experimentales et bacteriques. Arch. ital. de biol., 1892, xvii, 298; and Rif. med., 1892, viii.

Satterthwaite, T. E. Endocrinology and the heart. Med. Rec., 1920, xcviii, 510.

Schaposchnikoff, B. Zur Frage über Perikarditis. Mitt. a.d. Grenzgeb. d. Med. u. d. Chir. Jena, 1897, ii, 86–110.

Schwaer, G. Über Perikarditis exsudativa im Röntgenbilde. Fortschr. a.d. Geb. d. Röntgenstrahlen, Hamb., 1917, xxv, 24.

Sibson. Pericarditis. Reynolds's System of Medicine, Lond., 1877.

Soulie et Benhamon. Péricardite sero-fibrineuse et tumeur de mediastin. Paris méd., 1918, xxix, 313–316.

Sturges. The Lumleian lectures on heart inflammation in children. Lancet, 1894, 1, 583, 653, 723; also Brit. M.J., Lond., 1894, 1, 505, 561, 623.

Teeter, C. E. Heart irregularities; their clinical recognition and interpretation. J. Med. Soc. N. Jersey, Orange, 1920, xvii, 365–375.

Tice, F. A pericardiomediastinitis secondary to an acute plastic pericarditis. Med. Clin., Chicago, 1917, ii, 856.

Tornai, J. Neues diagnostisches Verfähren zur Konstatierung der Herzkrankheiten. Wien. klin. Wchnschr., 1920, xxxiii, 750–752.

Webber, O. Über das Wachstum und die Ernährungserfolge bei Kindern mit angeborenem Herzfehler. Monatschr. f. Kinderh. Leipz. u. Wien, 1920, xviii, 205–217.

Weiser, E. Ueber ein neues Symptom bei Tricuspidalinsuffizienz (Ophthalmus pulsans). Med. klin., Berl., 1919, xv, 1002–1004.

Williamson, C. S. Pericarditis with effusion. Experimental study. Arch. Int. Med., 1920, xxx, 206.

Willmore, W. S. Some recent advances in cardiology. Indian Med. Rec., Calcutta, 1919, xxxix, 81–86.

Wilson, M. G. Circulatory reaction to test exercises in children with heart disease. Med. Rec., N. Y., 1920, xcviii, 1919–1921.

Wilson, R. M., and Carroll, J. H. The nervous heart, its nature, causation, prognosis and treatment. London, 1919, H. Frowde, Hodder and Stoughton, p. 136.

Wolferth, C. C. Abnormal cardiac rhythms and their differentiation by simple methods. M. Clinics N. America, Jan., 1921, iv, 1207.

Yadama, M. Über die Bedeutung des Perikardiums. Mitt. d. Med. Faulkt. d. k. Univ. zu Tokyo, 1916–17, xvi, 527–537.

Young, J. J. Tricuspid stenosis and tricuspid insufficiency. New York M.J., 1920, cxii, 798–801.

Zondek, H. Herzbefunde bei endokrinen Erkrankungen. Deutsche med. Wchnschr., Leipz. u. Berl., 1920, xlvi, 1239.

Pericarditis and Endocarditis

Dieterich, F. H. A case of right-sided endocarditis (streptococcus viridans). Proc. N. York Path. Soc., 1920, xx, 5–9.

Mohr, T., und Bohm, L. Doppelseitige Embolie der Arteria centralis retinæ bei einem Fall von Endocarditis verrucosa. Berl. klin. Wchnschr., 1920, lvii, 1008.

Munzer, E. Endocarditis septica sive Endocarditis lenta (Schottmüller). Zentralbl. f. innere Med., Leipz., 1920, xli, 282-288.

Ohm, R. Ein Fall von Endocarditis ulcerosa maligna mit im Venenpuls erkennbarer und durch die Autopsie bestätigter hochgradiger Stauung der rechten Kammer. Ztschr. f. klin. Med., Berl., 1919, lxxxviii, 9-15.

Ruggeri, E. Endocardite maligna ad evoluzione lenta. Riforma med., Napoli, 1920, xxxvi, 522-525.

Salus, G. Streptococcus viridans bei Endocarditis lenta (benigna). Med. klin., Berl., 1920, xvi, 1107.

Wilson, F. N. The diagnosis of chronic myocarditis. Jr. Missouri Med. Assoc., St. Louis, 1920, xvii, 403-406.

Surgical

Adyne-Curran, W. J. P. Gunshot wound in the pericardium: pyopericardium with gas infection. Jr. Roy. Army Med. Corps, Lond., 1918, xxx, 599.

Bacigalupo, J. Mucodermoid cyst of the pericardium. J. Am. M. Assn., Chicago, 1918, lxxi, 961-963.

Boidin. Péricardite putride. Presse méd., Par., 1916, xxiv, 523.

Brauer, L. Die Kardiolysis und ihre Indicationen. Arch. f. klin. Chir., Berlin, 1903-04, lxxi, 258-267.

Camac, C. N. B., and Pool, E. H. Pericardiotomy for suppurative pericarditis following pneumonia. Tr. Ass. Am. Physicians, Phila., 1916, xxxi, 462-481; also Am. Jr. Med. Sc., Phila., 1917, cliii, 509-528.

Chackwitz, A. Agonale Franktur der Halswirbelsäule bei Herzschuss. Med. klin., Berl., 1920, xvi, 927.

Collins, A. W. Suture of the heart. Jr. Am. Med. Ass., Chicago, 1920, lxxv, 1271.

Curschmann, H. Zur Beurtheilung und operativen Behandlung grosser Herzbeutelergüsse. Deutsche Klinik, Berlin u. Wien, 1905, iv, 401-452.

Davis, C. B. Suppurative pericarditis; demonstration of a case one year after operation. Surg. Clin., Chicago and Phila., 1917, i, 375-380.

Delatour, H. B. Surgery of the pericardium and heart. Am. J. Surg., New York, 1909, xxiii, 114-121.

Delorme, E., et Mignon. Sur la ponction et l'incision du péricarde. Rev. de chir., Par., 1895, xv, 797, and 987; also 1896, xvi, 56.

Dock, G. Paracentesis of the pericardium. Brit. M. J., London, 1906, ii, 1026-1028.

Doliner. Eine seltene Projektilverletzung des Herzens. Ztschr. f. Medicinalbeamte, Berl., 1920, xxxiii, 97-100.

von Eiselberg, A. F. Über einen Fall von Incision des Herzbeutels wegen eiteriger Pericarditis. Wien. klin. Wchnschr., 1895, vii, 21-24.

Freese, E. M. Stab wound through both ventricles of heart with recovery. J.A.M.A., Feb. 19, 1921, lxxvi, 520.

Guillermo, M. L., y Montoya, J. M. Pericarditis supurada y pericardotomia. Repert. de med. y cirurg., Bogotá, 1917-18, ix, 115-126.

von Hofmann, E. Zur Chirurgie der Herzverletzungen. Deutsche Ztschr. f. Chir., Leipz., 1920, clvi, 175-234.

Kaminer, S., und Kondek, H. Herzbeutelveranderungen nach Lungenschüssen. Deutsche med. Wchnschr., Leipzig u. Berl., 1916, xlii, 668.

Klose, H. Über eitrige Pericarditis nach Brustschüssen und Extrapleurale Pericardiotomie. Beitr. z. klin. Chir., Tübing., 1916, ciii (Kriegschir, Hefte VI), 556-561.

Luckett, W. H. Removal of missile from the right ventricle of the heart with recovery. Surg., Gynec. and Obst., Chicago, 1920, xxxi, 417.

Morison, A. On thoracostomy in heart disease. Lancet, 1908, ii, 7 (Literature).

Morris, R. S., and Bader, E. R. A comparison of the percussion and roentgen ray findings after injection of the pericardium. Jour. Am. Med. Assn., Chicago, 1917, lxix, 450–454.

Quenu, J. Operation for bullet wound of heart: death from intrapleural hemorrhage. Paris méd., Jan. 22, 1921, xi, 76.

Rhodes, G. B. Intrapericardial traumatic hemorrhage; two unusual experiences in heart and pericardial surgery. Ann. Surg., Phila., 1917, lxvi, 44–49.

Shottuck. Pericarditis: Some points in its diagnosis and treatment. Transactions of Assn. of American Physicians, 1897, xii, 183.

Skirving, R. S. Remarks on a case of shrapnel wound of the posterior wall of the pericardium with an account of the operation for removal of the missile. Jr. Roy. Army Med. Corps, Lond., 1917, xxviii, 283–289.

Solaro, G. Contributo clinico alla sutura del cuore. Arch. ital. di chir., Bologna, 1920, ii, 283–309.

Summers, J. E. Cardiolysis: A further report with notes upon an additional case. Surg., Gynec. and Obst., Chicago, 1917, xxv, 92–95.

Tessier, J. P. La paracentese du péricarde par la voie posterieure. Bull. et mém. Soc. méd. d. hôp. de Paris, 3rd Series, xxxix, 413–416.

Thorburn, W. Cardiolysis (precordial thoracostomy) in heart disease. Brit. Med. Jour., 1910, i, 10.

von Walzel, P. R. Über Pericardiotomie. Mitt. a.d. Grenzgeb. d. Med. u. Chir., Jena, 1913, xxv, 264–277.

West, S. A case of purulent pericarditis treated by paracentesis and by free incision, with recovery. Statistics of paracentesis pericardii. Med. Chir. Trans., Lond., 1883, lxvi, 235.

Williamson, C. S. Purulent pericarditis (pyopericardium) with a discussion of pericardiotomy by Dr. Kellog Speed. Med. Clin., Chicago, 1916–17, ii, 907–918.

Medical

Admühler, F. Über die Actiologie der erworbenen Herzkrappenfehler. Deutsches Arch. f. klin. Med., Leipz., 1920, cxxxii, 279–284.

Alexander, J. S. A pericardial effusion of "gold paint" appearance due to the presence of cholesterin. Brit. M.J. London, 1919, ii, 463.

Billings, F. Clinical observations in pericarditis. J. Am. M. Assoc., Chicago, 1901, xxxvii, 1503–1507.

Bishop, L. F. Report of 1000 heart patients subjected to a complete cardiac examination with an account of the therapeutic results. Med. Rec. N. Y., 1920, xcviii, 508–510.

Blechmann, C. La dyspnée péricardique; le signe de Hirtz ou "signe des attitudes." Paris méd., 1912–13, xi.

——— Les épanchements du péricarde, étude clinique et thérapeutique; la ponction epigastrique de Marfan. Paris, 1913, J. B. Bailliere, p. 367, No. 172.

Brugsch, T. Praktische Digitalistherapie. Berl. klin. Wchnschr., 1920, lvii, 906.

——— Digitalistherapie. Deutsche med. Wchnschr., Leipz. u. Berl., 1920, xlvi, 933–935.

Brush, F. Convalescent treatment of heart disease by exercise applied through natural work and play methods. Med. Rec., Feb. 12, 1921, xcix, 253.

Calvert, J., and Pigg, T. S. Calcification of pericardium following suppurative pericarditis. Tr. Path. Soc., London, 1897–98, xlix, 31.

Calvert, W. J. Position of the heart in pericarditis with effusion. Johns Hopkins Hosp. Bull., Baltimore, 1907, xviii, 403–409.

——— A possible means of differentiation between cardiac dilatation and pericarditis with effusion. Arch. Int. Med., Chicago, 1909, iii, 92.

——— A possible differential sign between cardiac dilatation and pericarditis with effusion. J. Am. M. Assoc., Chicago, 1910, lv, 763–767.

——— Pericarditis with effusion. J. Missouri M. Assoc., St. Louis, 1906–07, iii, 389–392.

Christian, H. A. Clinic; pericarditis with effusion. Internat. Clin., Phila., 1918, 28th Series, iv, 23–37.

Cumington, C. W. Pericarditis following injection of antidiphtheric serum. Lancet, 1920, i, 1009.

Ebstein, W. Zur Diagnose der Flüssigkeitsansammlung im Perikardium. Archiv für path. Anat., 1893, cxxx, 418–443.

Eggleston, C. Some newer concepts in digitalis therapy. Am. J. M. Sc., Phila., 1920, clx, 625–639.

Ganter, G. Über die Aetiologische Bedeutung der Lues für die Aortenklappeninsuffizienz. Med. Klin., Berl., 1920, xvi, 821–823.

Gordon, A. R. Pericarditis with partial heart block. Univ. Toronto Med. Bull., Toronto, 1915, ii, 9–11.

Hufnagel, V., Jr. Le Duc Galvanisation bei Herzerkrankungen. Ztschr. f. phys. u. diatet. Therap., Leipz., 1920, xxiv, 92–94.

Jagie, N., und Schiffner, O. Über gonorrhoische Herzerkrankungen. Med. Klin., Berl., 1920, xvi, 976–978.

Klein, T. Case of mitral disease, auricular fibrillation and pulmonary tuberculosis. Internat. Clinics, 1921, i, 19.

LaFosse, P. Frottement péricardique dorsal au cours d'une endo-péricardite rhumatismale. Bull. et mém. de la Soc. méd. d. hôp. de Par., 1916, 3rd Series, xl, 1815–1817.

Lagrolet. De la compression du cœur dans les épanchements dupéricard. Thèse, Paris, 1878.

MacKenzie, J. Theory of disturbed reflexes in production of symptoms of diseases. Brit. M.J., Jan. 29, 1912, i, 147.

Mory. Ueber intravenöse Strophanthinanwendung in ihrem Verhältnis zur Digitalisbehandlung. München. med. Wchnschr., 1920, lxvii, 570.

Pearce, C. Cardiorespiratory mechanism in health and disease. Arch. Int. Med., Feb., 1921, xxvii, 139.

Perret, J. M. Pericardial effusion. U. S. Nav. Med. Bull., Wash., D. C., 1918, xii, 717.

Pietrkowski, G. Vorhofsdehnung und Digitaliswirkung. Deutsche med. Wchnschr., Leipz. u. Berl., 1920, xlvi, 937.

Riesman, D. Acute psychosis arising during course of heart disease. Am. J. M. Sc., Feb., 1921, clxi, 157.

Ritchie, W. T. Prognosis in certain affections of the heart. Lancet, Lond., 1920, ii, 643–645.

Rotch, T. M. Absence of resonance in the fifth right interspace diagnostic of pericardial effusion. Bost. M. & S. J., 1878, xcix, 389, 421.

Still, G. F. Observations on suppurative pericarditis in children. Pediatrics, New York, 1901, xii, 332–339.

Taussig, A. E. The inspiratory exaggeration of the dicrotic wave in pericarditis. Tr. Ass. Am. Phys., Philadelphia, 1914, 535–546.

Warthin, A. S. Accentuation of the pulmonary second sound an important sign in the diagnosis of pericarditis. Med. News, Philadelphia, 1895, lxvi, 395–399.

Willius, F. A. Congenital heart disease with complete auriculoventricular dissociation presenting unusual features. Boston M. & S. J., Jan. 20, 1921, clxxxiv, 64.

Adherent Pericarditis

Babcock, R. H. Adherent pericardium. J. Am. M. Ass., Chicago, 1901, xxxvii, 1578–1584.

von Bamberger, H. Über zwei seltene Herzaffektionen mit Bezungahme auf die Theorie des ersten Herztons. Wien. med. Wchnschr., 1872, xxii, 1–4; 25–28.

Bauer, L. Die Kardiolysis und ihre Indicationen. Arch. f. klin. Chir., Berlin, 1903, lxxi, 258–267.

Baumler, C. Errors in diagnosis of pericarditis. Deutsch. med. Wchnschr, 1920, xlv, 705.

Broadbent, J. F. H. Adherent pericardium. London, 1895.

Broadbent, Sir W. Adherent pericardium. Brit. M.J., London, 1898, i, 147–149.

BROADBENT, SIR W. An unpublished physical sign. Lancet, Lond., 1895, ii, 200.

BROADBENT, W. H., and BROADBENT, J. H. F. Heart disease and aneurysm of the aorta. New York, 4th Ed., 1906.

CABOT, R. C. Obliterative pericarditis, a cause of hepatic enlargement and ascites, with report of a case. Boston M. & S.J., 1898, cxxxviii, 463; 471.

CAMAC, C. N. B. Broadbent's sign. Johns Hopkins Hosp. Bull., Balto., 1898, ix, 271.

COOPER, C. M. The respiratory ratio; a preliminary note. J. Am. M. Ass., Chicago, 1909, lii, 1182.

DELORME. Traité de Méd., 1903, viii, 62.

DUROZIEZ, P. Signes de l'adhérence du péricarde. Bull. Soc. de méd. de Paris, (1880) 1881, xv, 60–69.

FIESSINGER, C. La Symphyse cardiaque. Rev. gén. de clin. et de thérap., Par., 1917, xxxi, 505; 521.

FRANÇOIS-FRANCK, A. Des bruits extracardiaques en général, et en particulier des bruits gastriques rythmés avec le cœur; contribution au diagnostic de l'adhérence du péricarde. Gaz. hebd. de méd., Paris, 1885, 2nd Series, xxii, 757–760.

FRENCH, H. Broadbent's sign of adherent pericardium. Gay's Hosp. Gaz., London, 1918, xxxii, 68.

FRIEDREICH, N. Über den Venenpuls. Deutsches Arch. f. klin. Med., Leipz., 1865–6, i, 241.

GAIRDNER, W. T. The favorable terminations of pericarditis, and especially in adhesion of the pericardium, with cases illustrating its secondary effects on the heart. Edinburgh Monthly Journal of Medical Science, 1851.

HARRIS, T. Indurative mediastinopericarditis, London, 1895.

HEAD, G. D. Chronic adherent pericarditis. (A study of 55 cases.) St. Paul M.J., St. Paul, Minn., 1905, vii, 251–259.

HOLST, P. F. Adhærent perikardium. Norsk. Mag. f. Lægevidensk., Kristiana, 1914, lxxv, 1105–1142.

KING, W. The harmlessness of adherent pericardium. London Lancet, 1845, ii.

KUSSMAUL, A. Über schwielige Mediastino-pericarditis und den paradoxen Puls. Berl. klin. Wchnschr., 1873, x, 433; 445; 461.

LAUCHE, A. Cystenbildung auf der Oberfläche des Herzens nach Pericarditis. Centralb. f. allg. Path. u. Path. Anat., 1919, xxx, 321.

LEHMANN. Pericarditis adhæsiva im Röntgenogramm; kasuistische Mitteilung. Fortschr. a.d. Geb. d. Röntgenstrahlen, Hamburg, 1905–06, ix, 196–202.

LYTER, J. A. Pericardium; adhesions, incidence, associated pathology and clinical diagnosis of chronic pericardial adhesions. Am. J. M. Sc., 1920, clix, 891.

MANGES, M. Adherent pericardium. Internat. Clin., Philadelphia, 1905, 15th Series, i, 1 and 67–73.

NOVE-JOSSERAND, G., et PÉHU, M. Sur un cas de symphyse cardique chez une enfant de 7 ans, remarquablement amélioree par une opération de Brauer. Lyon méd., 1914, cxxii, 1481–1485.

PICK, F. Über chronische, unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose) nebst Bemarkungen über die Zuckergussleber (Curschmann). Ztschr. f. klin. Med., Berlin, 1896, or 1895, xxix, 385–410.

RIEDER, H. Das Panzerberz. Fortschr. a.d. Geb. d. Röntgenstrahl., Hamburg, 1913, xx, 50–57.

RIESS, L. Über ein neues Symptom der Herzbeutelverwachsung. Berl. klin. Wchnschr., 1878, xv, 751.

——— Weitere Beobachtungen über eine die Herztöne begleitende Magenconsonanz bei Herzbeutelverwachsungen. Berl. klin. Wchnschr., 1878, xvi, 333.

RIETSCHEL. Pericarditis adhæsiva mit Leberschwellung, Milzschwellung und Aszites. München. med. Wchnschr., 1918, lxv, 1115.

SALVETTI, G. Contributo allo studio clinico della sinfisi del pericardio mell'eta infantile. Riv. crit. di clin. med., Firenze, 1915, xvi, 17, 33.

SEWALL, H. On a common form of reduplication of the first heart sound due to extracardiac causes. Am. J. M. Sc., Phil., 1898, cxvi.

SMITH, W. H. Chronic adherent pericarditis; a study of 62 cases. Jour. Amer. Med. Assn., 1913, lxi, 739.

STUERTZ. Zur Diagnose der Pleuraadhäsionen an Pericard. und Zwerchfell. Fortschr. a. e. Geb. d. Röntgenstrahlen, Hamburg, 1904, vii, 265–272.

TREMOLIERES, F., et CAUSSADE, L. Les phrenopéricardites adhesives. Presse méd., Par., 1918, xxxvi, 169–170.

WELLS, H. G. The pathology of the healed fibrous adhesions of the pericardium. Am. J. M. Sc., Philadelphia, 1902, cxxiii, 241–261.

——— The pathology of active tuberculosis of the pericardium. J. Am. M. Ass., Chicago, 1901, xxxvi, 1451–1458.

WENCKEBACH, K. F. Remarks on some points in the pathology and treatment of adherent pericardium. Brit. M. J., London, 1097, i, 63–68.

WILLIAMSON, C. S. Hemorrhagic pericarditis with acute septic endocarditis. Med. Clin., Chicago, 1916–17, ii, 918–927.

VAQUEZ, H., et BARDET, E. Étude radiologique de la symphyse cardiaque et des adhérences partielles du péricarde. Arch. d. mal. d. cœur, Paris, 1913, vi, 1–22.

VON DEN VELDEN, R. Rechtsseitige Cardiolyse. Zentralbl. f. Herzkrankh. (etc.), Dresden u. Wien., 1915, vii, 10–18.

VENUS, E. Die chirurgische Behandlung der Pericarditis und der chronisch-adhäsiven Mediastinopericarditis (Cardiolysis). Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Jena., 1908, xi, 401–416.

Tuberculous Pericarditis

BREITUNG. Über Pericarditis tuberculosa. Berl., 1877.

CARDARELLI, A. Pericardite adesiva tubercolori. Pensiero med., Milano, 1919, ix, 9.

——— Pericardite adesiva tubercolore. Riforma med., Napoli, 1919, xxxv, 2–4.

EMILE-WEIL, P., et LOISELEUR. Contribution a l'étude de la péricardite tuberculeuse; insufflation d'air dans le péricarde; pneumopéricarde et hydropneumopéricarde artificiels. Bull. et mém. Soc. de la méd. d. hôp. de Par., 1916, 3rd Series, xl, 1715-1730.

HARSHA, W. M. Tuberculous pericarditis. Internat. Clin., Phila., 1919, 29th Series, ii, 65.

OSLER, W. Tuberculous pericarditis. Am. J. M. Sc., Philadelphia, 1893, cv, 20–37.

RIESMAN, D. Primary tuberculosis of the pericardium. Am. J. M. Sc., Philadelphia & New York, 1901, cxxii, 6–21.

RODERICK, H. B., and CURL, S .W. A case of recurring effusion into the pericardial sac, probably of tuberculous origin. Lancet, Lond., 1919, i, 980.

THAYER, W. S. Observations on two cases of tuberculous pericarditis with effusion. Johns Hopkins Hosp. Bull., Balto., 1904, xv, 149.

WEIL, P. E., et LOISELEUR. Insufflation d'air dans la péricardite tuberculeuse avec épanchement pneumopéricarde et hydropneumopéricarde artificiels. Presse méd., Par., 1916, xxiv, 601–606.

Syphilis of the Pericardium

CLARK, O. Syphilis cardio-aortica de 35 annos de duracao (adjeo auriculare provocando crises de tachycardia paroxystical e insufficiencia aortica desde 1887). Brazil-med., Rio de Jan., 1920, xxxiv, 392.

DE STEFANO, S. Congenital heart defects and syphilis. Pediatria, Nov. 1, 1920, xxviii, 992; abstr. J.A.M.A., Jan. 22, 1921, lxxvi, 276.

LEREDDE. Premières recherches sur la syphilis cardiaque et son traitement; l'arythmie matinale. Bull. Soc. franç. de dermat. et syph., Par., 1920, xxvii, 89–107.

Letulle. Péricardite syphilitique. Bull. et mém. soc. Anat. de Paris, 1919, lxxxix, 402.

Marcek. Gumma of pericardium. Archiv für Dermatologie und Syphilis, Bd. xxv, S. 279.

Oddo, C., et Mattei, C. Étude anatomo-pathologique d'un cas de péricardite syphilitique a la période secondaire. Comp. rend. Soc. de Biol., Paris, 1920, lxxxiii, 223.

Phillips. Syphilis of the pericardium. Lancet, 1897, vi, 223.

Spalding, E. D., and von Glahn, W. C. Syphilitic rupture of a papillary muscle of heart. Bull. Johns Hopkins Hosp., Jan., 1921, xxxii, 30.

Pneumopericardium

Begtrup-Hansen, T. Pericarditis exudative tuberculosa pneumopericardium artificiale. Ugeskr. f. f. Læger., 1916, lxxviii, 1166.

Castex, M. R. Pericarditis purulenta aestreptococcus y pneumococos. Prensa med., Argentina, Buenos Aires, 1916–17, iii, Suppl., 65–68.

James, W. B. Pneumopericardium. American Medicine, 1904, viii, 23.

——— Trans. Assn. Am. Phys., 1904, xix, 351.

Lungdahl. Deutsch. Arch. f. klin. Med., Leipzig, 1913, cxi, 19.

Wenckebach. Zeitschrift für klin. Med., Berlin, 1910, lxxi, 402.

Hemopericardium

Treves, F. T. Suture of perforating wounds of the heart; death on the eleventh day. Lancet, 1906, ii, 706.

Whittaker. Twentieth Century Practice of Medicine, XIV, 50.

Abnormalities

Beneke, R. Über Herzbildung und Herzmissbildung als Funktionen primärer Blutstromformen. Beitr. z. path. Anat. u. z. allg. Path., Jena, 1920, lxvii, 1–27.

Chase, M. R. Congenital deficiency of the pericardium. J. Anat. and Physiol., Lond., 1915–16, l, 299–302.

Jacobson, V. C. Deviation of aortic septum: complete transposition of the great vessels, with report of 2 cases in infants. Am. J. Dis. Child., Feb., 1921, xxi, 176.

Keith, A., and MacDonnell, J. J. Case of transposition of viscera showing a potentially bicameral heart. Proc. Roy. Med. Soc. (Sec. Med.), Jan., 1921, xiv, 1.

Laubry, C., and Pezzi, C. La persistance du canal arterial; étude pathogenique et clinique. Arch. d. mal. du cœur, etc., Par., 1920, xiii, 145–167.

Meyer, E. Zur Kenntnis des kleinen Herzens. Deutsche med. Wchnschr., Leipz. u. Berl., 1920, xlvi, 789–791.

Müller, H., Jr. Patent interventricular septum. Deutsches Arch. f. klin. Med., Sept., 1920, cxxxiii, 316; and March 19, 1921, lxxvi, 827.

Radi, R. Di un vizio congenito del cuore. Boll. d. clin., Milano, 1900, xxxvii, 108–120.

Rominger, E. Ein Beitrag zur Diagnostik angeborener Herzanomalien. Montatschr. f. Kinderh., Leipz. u. Wien., 1920, xviii, 417–423.

Weber, F. P. Interesting cases in which a so-called Chiari's net was found in the right auricle of the heart, with or without the presence of any other congenital cardiac abnormality. Internat. Clin., Phila., 1920, 30th Series, iii, 43–51.

Electrocardiography

Assman, H. Über Veränderungen der Hilusschatten im Röntgenbilde bei Herzkrankheiten. Deutsches Arch. f. klin. Med., Leipz., 1920, cxxxii, 335–361.

Bishop, L. F. Localized changes in the heart muscle as determined to be in the right bundle branch by the electrocardiograph. Proc. New York Path. Soc., 1920, xx, 70–87.

BRUNWIN, A. D. Electrocardiography on active service. Practitioner, March, 1921, cvi, 183.

DAVIS, J. S., and UNDERWOOD, G. M. The use of the electrocardiograph in the diagnosis of difficult heart cases. Texas State J. M., Fort Worth, 1920–21, xvi, 206–210.

FAHR, G. Some fundamental principles of electrocardiography. Arch. Int. Med., Jan., 1921, xxvii, 126.

FRIDERICIA, L. S. Die Systolendauer im Elektrokardiogramm bei normalen Menschen und bei Herzkranken. Acta Med., Scandin., Stockholm, 1920, liii, 469, 489.

HESS, W. R. Die graphische Aufzeichnung der Herztone nach neuer Methode. Arch. f. d. ges. Phyl., Berl., 1920, clxxx, 35–60.

KRAUS. Zur Deutung des Elektrokardiogramms. Berl. klin. Wchnschr., 1920, lvii, 917–920.

ROUTIER, D. Étude analitique sur l'emploi du condensateur en électrocardiographie. Arch. d. mal. du cœur, etc., Par, 1920, xiii, 17–23.

——— Étude experimentale de l'action du condensateur sur l'électrocardiogramme. Ibid., 174–176.

SCHOTT, E. Elektrokardiographische Studien bei akuten Vergiftungen. Arch. f. exper. Path. u. Pharmakol., Leipz., 1920, lxxxvii, 309–341.

SEHAM, M. Electrocardiogram in normal children. Am. J. Dis. Child., March, 1921, xxi, 247.

WEBER, A. Über das Kardogramm. Ztschr. f. exper. Path. u. Therap., Berl., 1920, xxi, 252–262.

CHAPTER V.

ANGINA PECTORIS

By Alexander Lambert, M.D.

Definition, p. 253; Etiology, p. 253; Symptomatology, p. 259; Diagnosis, p. 265; Complications and sequelæ, p. 267; Association with other diseases, p. 267; Clinical varieties, p. 267:—Angina sine dolore, p. 268; Pseudo-angina, p. 269; Toxic anginas, p. 269; Abdominal angina, p. 271;—Treatment, p. 272; Prognosis, p. 276; Pathology, p. 277; Historical summary, p. 278.

Definition.—Angina pectoris is not a disease in itself but is best defined as a symptom complex characterized by pain in the chest which may be of the uttermost intensity, rarely failing to convey with it the fear or the conviction of impending death. Angina pectoris kills through the vagal inhibitory mechanism in the heart. The original morbid process which sets in motion the fatal cardiac inhibition is of varied origin.

Etiology.—Medical opinion regarding the causation of angina pectoris has varied during the last century and a quarter, since Heberden first called attention to this group of symptoms, according to the changes in fashion of medical theories. At first, it was produced by spasm rather than inflammation. Later, it was a question of arterial pressures and tension. At one period, the discussion hinged around the differences in the coronary blood supply and the spasm or intermittent claudication of these arteries. At another period, some unknown conditions of exhaustion or disease of the myocardium have sufficed to explain the symptom complex. Running through it all was the urgent necessity in the medical mind of finding the definite pathologic lesion to explain the group of symptoms which could so suddenly appear without previous warning in a man in vigorous health, and in many instances be so quickly fatal. That disordered function or a perversion of a normal function could kill without concrete pathologic lesion did not seem possible. Huchard has collected the various ideas of many physicians from different periods and gives some sixty-four different opinions to explain the causation of angina pectoris. Since Edward Jenner, the friend of Heberden, found that in most patients dying of angina, the coronary arteries were diseased, coronary disease has usually been considered as the underlying cause of the pain and cessation of cardiac action. This has been generally accepted in spite of the fact that postmortem examination showed that the majority of patients with diseased or calcareous coronaries had not suffered during life any symptoms of angina pectoris and in many patients who had died of angina, the myocardium was practically normal and the coronaries healthy. The Viennese school of Bamberger and Von Neusser has for many years insisted that the symptom complex had as its foundation some morbid process which set in motion the sensorimotor arc of the vegetative nervous system involving the mechanism of the heart's action.

The separation of diseases of the heart from diseases of the bloodvessels in medical teaching and thought, has also retarded an appreciation of the correct interpretation of the anginal complex. In the minds of most observers, both laymen and physicians, the intense precordial or substernal pain often accompanied by cessation of the heart's action could only be conceived as due to a disease of the heart itself. Among the valuable contributions which Mackenzie has made in the study of the heart and circulation, is the conception of the sensorimotor reflex as a means through which the viscera express in terms of pain certain disturbances of function or morbid changes in their tissues. We do not to-day know what pain is in the final analysis but we do know that both the vegetative nervous system, and the cerebrospinal system of nerves possess fibers which, going through the posterior root of the spinal nerve, produce a sensation in consciousness, which we call pain. In the vegetative nervous system, this reaction in the sensory fibers causes a return outflow of nerve action in either or both neural systems which results in definite motor responses, producing increased or diminished function in somatic muscles or viscera, or often cessation of all function. Whether we accept the myogenic or neurogenic action as the origin of cardiac function is of no consequence, since, in either case, the sympathetic portion of the vegetative nervous system possesses motor power to increase enormously the cardiac action or the autonomic portion through the vagus can slow down its mechanism or inhibit all action. It is only through some such general conception as this that one can explain the varied pathologic findings in those patients who have died showing the symptom complex of angina. The most common lesion found postmortem is that of an aortitis in the first portion of the ascending aorta. In about one-third of the cases the coronary arteries are definitely stated to have been healthy and not diseased. In most cases the myocardium has shown various forms of myocardial disease or degeneration. In many instances, however, this too has been reported healthy and not diseased. Morison reports attacks of angina occurring in a patient who showed on postmortem examination an intravascular aneurysm of the right coronary artery. Pericarditis is also another causal factor in producing angina pectoris, especially pericarditis which occurs around the base of the heart involving the insertions of the great vessels, especially the aorta. Sir Clifford Allbutt reports a case in which no lesion was found except inflammatory adhesions around the root of the aorta from a previous attack of pericarditis. Von Neusser reports the case of a patient who, two years after rheumatism, showed typical signs of angina pectoris and the postmortem examination showed only adhesions of the heart to the pericardium, while the coronaries and the aorta were absolutely normal at their origins. Von Neusser also reports a case of angina pectoris in which there was a tumor on the left vagus and on the right phrenic nerve, with a similar tumor growing on the large cardiac nerve, and the heart, except for being "flabby," showed no lesions. Death has occurred in a paroxysm of angina pectoris as reported by several observers, both in young patients with normal hearts and in old patients with diseased hearts, during the passage of gall-stones. It is not an uncommon occurrence for an obliterating thrombosis of the various arteries of the coronary system to occur, bringing on the most terrific attacks of anginal pain, in which death not infrequently occurs. Other patients, it is true, have thrombosis of the coronary arteries without pain and die therefrom. Still others go on living in spite of coronary thrombosis. Verdon claims that the exciting cause of the symptom complex of angina pectoris is due to spasm of the gastro-esophageal portion of the alimentary tract or to some undue traction on the esophagus as from an over-distended stomach. This author believes that the symptom complex is an expression of a segmentary neurosis in the cord, the inflammation of each neuron or the neuronitis, as he expresses it, being proven by the persistent areas of peripheral pain and tenderness in the skin in various areas on the chest wall, so noticeable in many patients who suffer the attacks of lesser intensity of angina, or even in those who suffer from severer attacks. Other cases are reported where inflammation around the celiac axis and the abdominal aorta had given rise to attacks of anginal pain. Vasquez and Balfour have both expressed the belief that the pathological dilatation of the cardiac muscle produces, in some instances, attacks of angina. The pain occurs as the left ventricle dilates, but this is not a universal observation, for it has been a noticeable feature in certain patients suffering from attacks of anginal pain, that when their heart had dilated the attacks of pain ceased, and Musser among others, has reported a patient in whom the attacks of pain ceased when the heart had dilated, but reappeared when the cardiac muscle had sufficiently recovered to overcome its dilatation. It is evident therefore that the symptom complex of angina pectoris accompanies many morbid conditions which have as a pathologic basis equally varied lesions. The one common factor in all the different lesions is the possible involvement of the sensory fibers of the vegetative nervous system, thus setting in motion the sensorimotor reflex producing the symptom complex of angina pectoris.

The clinical outbreak of angina pectoris occurs most frequently in men at the time of life when senescence has begun but before senility is established. It occurs, therefore, most frequently when arteriosclerosis has begun and the health of middle age has begun to wane. When once old age is established with calcification of the coronary arteries, the symptom complex of angina does not so frequently occur. Angina shows itself as a symptom complex of rheumatic aortitis even in childhood or in youth or it follows an attack of influenza from an aortitis which may occur in youth, in middle life or old age. It very frequently follows the infection of syphilis when that disease attacks the aorta, producing an aortitis or an aneurysm. It follows, therefore, those forms of aortitis in which the vasa vasorum are the channels through which the inflammation proceeds in the adventitia and through it to the media producing a mesarteritis, in which the intima is only secondarily involved. When once the morbid basis which starts the anginal reflex is established in aorta or heart, the attacks may be produced by any undue exertion or even by the slightest exertion which upsets the existing equilibrium in which pain is not present. A sudden increase of blood-pressure produced by exercise, particularly a slightly increased rapidity of walking after a meal or walking against the wind or up a distinct grade or ascending stairs, are all sufficient to start the reflex into activity. It may follow any exciting emotions or it may follow the acts of defecation or of coitus. A person who is in such unstable equilibrium is in danger from any excessive emotion and especially from anger or excessive joy. The pain of angina pectoris follows also the intoxications of tobacco, lead, gout or diabetes. Whether in these instances it is due to true intoxication as from tobacco or whether it is produced by arteriosclerosis which accompanies these other conditions cannot be said with certainty. Tobacco, according to Huchard, produces lesions in the aorta and also attacks of angina without visible tissue changes. Most clinical observers agree, however, that when once aortitis is present, tobacco increases both the frequency of the occurrence and the severity of the anginal complex. Valvular diseases of the heart are not as a rule accompanied by the anginal complex of symptoms. Lesions of the aortic valve which are naturally extensions of the disease processes in the aorta, are the lesions with which angina is most often evident. Mitral stenosis, however, is sometimes accompanied by attacks of true anginal pain and these occur in patients in whom postmortem examination shows healthy coronary arteries. Beginning aneurysms of the aorta are also at times accompanied by anginal pain due in all probability to the same reflex mechanism which produces angina in the mesarteritis without the aneurysmal sacculation or dilatation.

Sir Clifford Allbutt is correct in his contention that the most frequent underlying morbid process of angina pectoris is an aortitis in the subsigmoidian area of the aorta. He does not, however, seem satisfied to accept the fact that Manouelian and others have demonstrated sensory endings of the nerve fibrils in the aorta, adventitia and media, but believes that there must be present pacinian nerve-endings of sensory nerves to account for the sensory reflex being set in motion. These pacinian nerve-endings have not yet been proven to exist in the aorta but they have been found in other blood-vessels. Physiologists are beginning to ascribe sensory functions in nerve-endings in the abundant nerve supply to the sinuses of Valsalva at the commencement of the aorta and around the auricular ventricular orifices. Recent investigators also show nerve fibers and ganglia scattered through the heart, and some investigators claim to have found sensory nerve-endings in the heart itself. The enervation of the heart and the aorta and the sensory paths from these regions are not finally worked out but the evidence seems sufficient to justify the belief of the existence of a sensorimotor reflex produced by the nerves running from and to the heart in the sympathetic and the vagus systems. There is no question but that the distribution of pain in the anginal attacks can be explained by the anatomical distribution of known nerve fibers. The idea that angina pectoris is of nervous origin and not of muscular or vascular causation is not new. It has been held in France by Bouillaud and Desportes; by Rombert in Germany; by Bamberg and Von Neusser in Vienna. Sir Clifford Allbutt, who most energetically denies either vascular or muscular origin and who has put aside all theories of nervous origin, falls back in his final analysis on an aortitis or an inflammatory process giving rise to an involvement of sensory nerve-endings and acknowledges that only through sensory nerve-endings is the painful reflex set in motion. His explanation, therefore, is one of nervous etiology of angina pectoris, especially since in some instances of aortitis produced by the same inflammatory processes anginal attacks do not occur. Vasquez divides the etiology of angina pectoris under two heads: (1) That of angina produced by effort, and (2) the angina of repose. The former follows exertion and is due to lesions in the aorta, especially in the subsigmoidal area. The latter occurs during sleep and in Vasquez' opinion, the painful reaction follows a distention of the left ventricle and secondarily of the aorta, the idea being that the left ventricle as well as the aorta, surprised suddenly by hypertension is distended excessively and the excitation of the nerve filaments of the myocardium, in consequence, is transmitted to the cardiac plexus producing the symptoms of angina pectoris. The theory often accepted that the pain is produced by spasm or by anemia of the cardiac muscle seems highly improbable especially since, in many cases of even severe attacks of angina, the pulse does not vary in frequency, force or tension until just before death. In angina due to coronary thrombosis, the pulse is often very rapid and may be irregular or small and feeble, but coronary thrombosis is not the usual lesion underlying the anginal attack. If there were a spasm of the muscle, or if there were deviation from normal in its contracting power, it would seem most probable that there would be evidences of it in the pulse. Moreover, the cardiac muscle does not go into tetanic spasm in the manner of a skeletal muscle. Irregularity of the conducting mechanism would show in irregularity in the pulse and while this sometimes occurs, the contracting system of the myocardium is the only mass which would influence the force of the pulse. Moreover, if the heart contracts, it does so with all its vigor under Bowditch's law. The same is true of intermittent claudication of the coronary arteries causing anemia of the myocardium. All cardiac pain is not of a single origin and the morbid processes which produce myocardial exhaustion or disease do not account for the intensity or kind of pain evident in anginal attacks. These processes in the myocardium produce dyspnea and breathlessness but do not produce the anginal pains. The absence of dyspnea is a striking fact in the symptom complex of angina pectoris. Von Neusser draws attention to the fact that in intermittent claudication of the peripheral arteries there must be a spasm of the muscles of the media as well as stenosis of the lumen and whether it is through the hypertrophied layer of the muscular coat or through the irritation of nerve-endings, the pain produced is caused as much by this as by the anemia brought about by the stenosed lumen of the vessels. Pain is caused in intestinal spasm by the irregular contraction of the muscular layer of the gut, as in colic or pylorospasm, and it may be that in the aorta with a diseased media there may be areas of irregular contraction, even if not of spasmodic tension, which in some instances produce the pain. Mackenzie reports a case in which the arterial pressure was 190 during the attack. Nitrites relieved the attack and some minutes after, when the patient was comfortable and free from pain, the pressure had risen to 200. It was, therefore, not the pressure but some added element which produced the attack of angina. Nitrites relieve the spasm by inhibiting the vasoconstrictor nerves. It is, therefore, not improbable that in many instances we are dealing with some tension in the muscular layer, involving the sensory nerve-ending, of the aorta which brings about this intense pain.

There is no question but that diseased coronary arteries and the diminution in the lumen of the coronaries is in all probability a very great factor in the immediate causation of death, but death in one-third of the cases that have come to postmortem has occurred with healthy coronaries and in many instances with healthy cardiac muscles.

That the sensorimotor reflex may start equally from the aorta or the heart, the clinical evidence is conclusive. Both the heart and the aorta are amply supplied with nerves from the sympathetic and vagus systems. Besides the sympathetic vasomotor nerves the aorta is supplied by both vagus and sympathetic nerves from both the superficial and deep cardiac plexuses, particularly around the aortic root at the junction with the heart. The right and left coronary plexuses not only surround the opening of each coronary artery but spread around on the adjacent areas of the aorta as well, and both these plexuses receive fibers from both the superficial and deep cardiac plexuses. The depressor nerve in animals, such as the rabbit, described by Ludwig and Cyon is an afferent nerve. Its homologue in man is described by Tandler as descending separately or in the sheath with the superior cardiac sympathetic nerve and is made up from the upper heart branches of the vagus and by a branch from the external branch of the superior laryngeal nerve of the vagus. It spreads out and terminates upon the aorta, not going to the heart itself. Its function seems to be to carry to the sympathetic ganglia those stimuli necessary to regulate the vasomotor control and the rise and fall of blood-pressure through reflex stimulation of the splanchnic area and abdominal vessels.

It is believed that the vagus contains constrictor nerves going to the coronary arteries. An accurate description of the entire afferent tracts of the sympathetic nerves cannot be given. It is at present unknown.

The sensory motor reflex arc, however, is present and one expression of its efferent action is seen in the vagal inhibition of the heart. The condition of the coronary vessels, probably, or of the myocardium may turn the scales for life or death. Hearts which possess healthy muscular systems and undegenerate coronary vessels resist best the vagal inhibition and a healthy heart will often overcome the attack even though it be serious, but a heart crippled in its blood supply or in its myocardium, has lost its power to overcome the fatal inhibition. The conducting system of the heart possesses a vascular supply separate from the general muscular mass of the heart but we must look to the future to show the differential diagnosis indicating when this branch of the right coronary artery is cut off from its blood supply. Even, however, in hearts not crippled by disease and possessing the resiliency of youthful tissue the recuperation of healthy cardiac muscle with normal vessels may fail to occur, and the reflex inhibition may cause a permanent cessation of all cardiac action.

Symptomatology.—The chief and most characteristic symptom of angina pectoris is pain. This is usually a substernal pain at the right or left of the sternum about the level of the third rib, or it may be under the manubrium or it may be under the xiphoid. The pain begins as either sharp and stabbing or tearing, or as a dull grinding pain that carries with it the feeling as if the chest were being held and then crushed in. The pain usually radiates upward to the shoulder or back under the left scapula, and if going to the shoulder, it continues on down the arm to the elbow or, following the ulna nerve, ends in tingling pain in the fourth and little fingers. At times the pain is only localized in the wrist or may appear as a burning ache on the inside of the upper arm or it sometimes remains in the arm and is not felt in the chest. Sometimes, it begins in the arm and goes upward and on to the chest. Usually, however, it starts in the chest and goes down the left arm. In the majority of cases it radiates to the left but it may, however, radiate to the right arm or simultaneously to both arms. In dextrocardia, the pain is still on the left side. The pain may not go towards the arm. In some individuals it begins in the third space or in the center of the chest, goes up along the vessels of the neck and ends as an intense gripping pain in the constrictor muscles of the pharynx or in the notch between the mastoid process and the jaw, driving the pain into the ears or on the side of the neck, or it radiates into the face or jaw itself along the second and third branches of the fifth nerve. It may shoot out from the chest to the left shoulder and the top of the trapezius. In three persons in the experience of the author, the pain has been most severe in the third left intercostal space and in the insertion of the accessory nerve on the left in the trapezius and also in the great occipital nerve in the back of the head. In other patients the pain radiates down the leg. Osler and Huchard report cases where the pain radiated down into the testicle and was followed by swelling of the testicle. Sometimes the pain begins in the back and then passing to the front, follows the usual course of left radiation in the arm. A division is sometimes made of a special kind of angina pectoris in which the pain begins in the epigastrium and is designated as abdominal angina.

To understand the symptoms of pain and its distribution and varying radiation in angina pectoris, one must remember clearly the anatomical description of the sympathetic and vagus nervous systems. The vagus nerve as it issues through the jugular foramen, sends off from the jugular ganglion an auricular branch going to the drum, to the external auditory meatus and to the auricle of the ear. It is through this nerve that anginal pain is carried to the ear. This nerve is considered to be associated with the trigeminus and accounts for the pain in some instances occurring in angina, in the jaw itself and in the teeth. The tenth nerve or vagus proper is a sensory nerve to the pharynx, esophagus and stomach and respiratory organs. This is joined at its ganglion nodosum by the accessory or eleventh nerve, which carries the motor nerves to the vagus and then goes to the palate and the pharynx and the respiratory organs, and carries the inhibitory fibers of the heart. It is through the pharyngeal branches that the gripping spasm in the throat is so intensely felt in anginal attacks. It is also the motor nerve for the alimentary canal. It is the motor nerve to the upper portion of the trapezius and the sternomastoid muscles. These last two muscles embryologically are derived in part from the branchial arches and formerly belonged to the respiratory group. Tenderness and hyperalgesia are very commonly present at the insertion of the branches supplying these muscles following an attack of angina. From the ganglion of the root of the vagus, a nerve goes over and joins the connecting branch of the second and third cervical nerves. It is probable that through this nerve pain extends back of the ear over the neck and scalp in either the great auricular nerve to the side of the neck, or on to the upper portion of the ear itself by the little occipital nerve, or along the back of the head through the great occipital nerve, extending by this nerve over the scalp to the crown of the head. Radiation in this area cannot be infrequent, as in the author's experience it has been very definitely evident in three patients. The gripping spasm of pain in the throat in some attacks of angina pectoris, which have come under the author's observation, occurs most frequently in those cases of angina which occur with diseases of the aorta.

As the vagus descends into the neck it sends off branches from the main trunk to the heart and also cardiac branches from the superior and inferior laryngeal nerves. These branches pass to the cardiac plexuses, the upper cardiac branches of the left vagus and fibers from the left lower cardiac nerve forming the superficial plexus with the left superior sympathetic nerve. The deep cardiac plexus is formed by all the other nerves coming from the vagus and the sympathetic. These two plexuses anastomose with the esophageal, bronchial, and anterior and posterior pulmonary plexuses and are the pathways through which the inhibitory action on the heart occurs in operations of the pleura and lungs. The sympathetic nerves come down into the neck from the superior ganglion from the middle sympathetic ganglion when present, and from the inferior ganglion when this forms a separate ganglion or joins with the first thoracic ganglion to form the stellate ganglion. The sympathetic nerves coming from the upper five thoracic nerves go up and join the sympathetic cord in the neck. The lower thoracic sympathetic nerves, although distributed chiefly in the abdomen, send some of their fibers directly to supply the lungs, aorta and esophagus. The accelerator fibers of the heart are efferent sympathetic fibers emerging from the spinal roots of the second, third and fourth thoracic spinal nerves. It is also said that some of these fibers may be found in the first and fifth thoracic and often in the lower cervical nerves. They pass then, by way of the white rami to the first thoracic ganglion and thence to the lower cervical ganglion and are given off from the loop of Vieussens, going from there to the cardiac plexus. No accelerator fibers are found above the inferior cervical ganglion. The cardiac inhibitory center is that of the nucleus ambiguus from which rise the motor fibers for the vagus and the glossopharyngeal nerves. The vagus also carries afferent fibers through the abdominal viscera and the heart may be reflexly inhibited most readily by the stimulation of the surface of the abdominal viscera or by a blow thereon or by sudden distention of the stomach. The radiation in the cervical nerves is to the second and third segments as just mentioned. Then, skipping the fourth, fifth, sixth and seventh segments, the pain follows the inner aspect of the arm in the segments of the eighth cervical and in the first and second thoracic. On the chest wall from the first to the eighth thoracic segments, especially the regions supplied by the third and fourth thoracic, are the areas showing sensitiveness and pain from the cardiac reflexes. The pain is therefore distributed in the areas supplied by the intercostobrachial, the medial cutaneous of the arm and of the forearm and the ulna nerves. Radiation downward probably must go from the aortic plexus through those nerves coming up from the lower thoracic fibers. A branch from the twelfth thoracic nerve enters frequently into the formation of the lumbar plexus and the genitofemoral nerve is formed by a branch of the first and second nerves of this plexus. From this genitofemoral nerve a small external spermatic branch is given off. It is probably through the branch to the spermatic plexus of this nerve that the unusual distribution of the anginal reflex has been observed to extend to the testicle. The internal sphincter of the rectum is supplied by both thoracic fibers of the sympathetic system coming down through the inferior mesenteric ganglia and sacral fibers of the vagal system coming to it through the second, third and fourth sacral nerves. The inferior hemorrhoidal branch of the pudendal nerve also sends fibers to the sphincter. The sensorimotor reflex has pathways here for its conduction through thoracic connections. But probably straining in the act of defecation more often produces anginal attacks similar to these produced by exertion, especially in patients in whom the paroxysms start from slight exertions. The attacks of angina occurring so frequently in elderly men during coitus may arise through reflexes produced in the vegetative nerve fibers in the branches of the pudendal nerve to the external genitals. But most probably emotional excitement and physical exertion play a large part in originating these anginal attacks.

The patient seized with an attack of angina pectoris stops where he is. He is usually found sitting or standing perfectly still with his hands and arms pressed to his sides rigidly holding himself, fearing even to breathe lest he increase the pain. Often he is found with his hand grasping his upper arm or wrist or pressing against his chest where the most intense pain seems to be centered. He may cry out with the intensity of the pain, and a few roll about in agony. The face becomes pale and looks pinched and drawn and the perspiration starts from the forehead and runs down the face. In some there is an abundant flow of saliva into the mouth which even may overflow and run out of the sides of the mouth and over the chin. With this intense pain there comes the fear of approaching death, or, in many patients as expressed by them, it is more a certainty of approaching dissolution than the fear of it, for it does not seem to them that they can suffer more and still live. Or, the feeling may be one of intense apprehension or anxiety. In some patients there is a feeling of globus with the sensation that could they but rid themselves of a mass of gas from their throat or stomach they would be relieved and in many patients there frequently is an eructation of gas or vomiting or large amounts of flatus are passed from the bowel. In some attacks the pain during the attack lasts but a few minutes and subsides as suddenly as it arises. In other instances, the attack may subside but may recur on very little exertion on the part of the patient and this condition may continue for many hours. In the mild attacks the pain does not reach its full intensity, for the patient appreciates the warning and stops whatever he is doing. Usually the pain in the chest subsides first, then the arm pain ceases, but numbness disappears more slowly. Those patients in whom angina is brought about by exertion can stop walking, if that be the cause, and wait until the pain ceases and then go on, and gradually, the heart, becoming accustomed to its increased work, can perform it without giving the distress. After an attack of anginal pain, there is often left an area on the chest wall of hyperalgesia. This is particularly common over the pectoral muscle and along the anterior axillary line, sometimes extending upon the inner side of the arm. It is also not uncommon to find a tender spot over the third rib on either side and in the sternomastoid or trapezius muscles where the accessory nerve enters. Verdon describes cases of angina in nervous high-strung women who were having frequent attacks and in whom the variation of the areas of tenderness as they appeared in the intercostal spaces occupied different areas from time to time in front and behind on the chest wall. These patients often showed points of tenderness over the dorsal processes of the vertebræ. The intensity of the pain is not always in proportion to the gravity of the attack. Mild nagging attacks may be the forerunners of the severest forms, or severe attacks may subside and cease to recur. In the very gravest forms of angina there may be almost absence of pain and patients dying quickly often do not seem to suffer the full intensity of agony. There is a form of angina without pain usually designated as *angina sine dolore,* in which the patient shows the cardiac weakness and collapse and the anguish with the fear of death but with no pain.

In many cases the pulse remains normal and the heart does not quicken its rhythm. Often in the most intense attacks the heart beats quietly in its normal rhythm until the vagal inhibition starts, often suddenly. In other attacks the pulse becomes full though regular and may beat as low as 28 or 30 to the minute. In these cases the heart feels to the patient as if it were bursting or had stopped suddenly and was still. The pulse may be rapid and feeble or small and tense, especially in those cases where there is coronary thrombosis. In some cases it may be slightly increased in frequency. It is sometimes reported as being small, soft and compressible or small and tense. In other cases, extra systoles have been known to occur. In some patients with cardiac insufficiency and arhythmia between the attacks, the pulse becomes regular during the paroxysms and cardiac murmurs have also been noted to disappear during the paroxysm. In some patients there has been noted a surprising smallness of the left radial pulse as compared with the right. This peculiarity may exist in patients without the existence of aneurysm. The respiration is usually but little affected. It is characteristic of the pure uncomplicated cases of angina pectoris that there is no sign of dyspnea but, on the contrary, apnea is present. Patients at times will take a long breath and hold it in order to inhibit any possible movement of the chest that might in any way increase their pain. The usually normal pulse and lack of dyspnea distinguishes true anginal attacks from both cardiac asthma and the dyspneic attacks of chronic cardiac diseases. After the angina attacks have extended for some length of time, cardiac dyspnea may come on. In the coronary thrombotic cases of angina there may be a definite sense of shortness of breath and some evidence of dyspnea. In these protracted cases of angina pectoris, cyanosis and pulmonary edema with bloody expectoration may occur. In some patients it is reported that they suffer from alternating attacks of dyspnea and true angina. Between attacks of angina, Cheyne-Stokes breathing is met with, particularly between very severe attacks.

The symptom complex of angina is characterized as much by the horror of immediate death as by the intensity of the pain. In the extreme degree, the conviction of impending dissolution is said to be almost peculiar to angina pectoris. Often in the first attack, even when this is not of great intensity, there is a peculiar creepy horror in consciousness that the number of one's days is fulfilled. It has been variously described as a conviction that death is imminent, rather than a fear of dying. Death seems inevitable and inescapable and one therefore waits in benumbed agony for it to come and blot out the suffering. The severity of the pain and the intensity of the horror do not run parallel. Often with slight or minor attacks of angina the horror is the striking feature of the paroxysm or the reverse may be true; there may be intense pain and yet no fear of death. Allbutt says that in his experience, in young persons the horror is less manifest and often absent. It seems in older persons, that this shadow may even obscure the pain and that many of these sufferers dread more this death portent than even the terrible pain. The same patient may suffer in one attack more anguish than pain and in other attacks more pain than anguish. Or, either pain or anguish may be entirely absent in any attack in the same patient. In some patients only the pain occurs and the horror never develops and this even in elderly people. In false angina, the conviction that death is undoubtedly near does not come to the sufferer, but there is a terrifying fear that the pain may be that of angina and if so, that death may occur. These patients are afraid of the idea of angina pectoris lest they suffer sudden death.

There is a widespread idea among the profession that the attacks of angina are dependent upon the height of the blood-pressure. Nothnagel's angina vasomotoria is based on this idea in which the spasm of the peripheral vessels becomes so great that the heart, unable to overcome the pressure in front of it, suffers from an attack of pain. The relief by the nitrites has been laid to the reduction of the blood-pressure. Mackenzie reports a case with a blood-pressure at 190 in which he stopped the anginal seizure by giving amylnitrite and some minutes later he found the blood-pressure to be 200. The author has taken blood-pressures in attacks of true angina and found them to be between 130 and 140, which was the height that had been found in the patient the day before the attack and for some weeks previously. Vasquez and other observers report the occurrence of the anginal symptoms in patients with high, low or normal blood-pressures. The blood-pressure itself is, therefore, not necessarily a factor of causation. Patients with high blood-pressures seem clinically, however, to be in much more unstable equilibrium than those with lower pressures and more easily start the painful reflex into action. Neusser reports the case of a patient who did not show any increased pulse during the intervals nor increased blood-pressure during the paroxysms. He also speaks of numerous cases in which the blood-pressure decreased during the stenocardiac paroxysm. He also reports one case in which the blood-pressure was 90 previous to the attack and equally low during the attack. The attack ceased when, through digitalin and theocin the blood-pressure rose to 110 but the dyspnea and cephalalgia persisted. Neusser explains the difference as depending upon the localization of the vascular spasm; if this involves the regulating splanchnics, a marked increase in the blood-pressure may take place. If, however, it is localized in the thoracic region, the paroxysms may be accompanied by a vasoconstriction of the vessels of the upper extremities and of the coronary arteries. If the latter be true, the nutrition of the heart would be reduced and the heart cause a decrease in the blood-pressure.

The patient's face during the attack may be very pale and sweaty, or it may be flushed and as the attack proceeds the vessels of the neck may bulge and throb. Intense sweating may occur over the body and on the hands as well as on the face, and be of great intensity; Osler speaks of one patient's hands being as parboiled as a washwoman's.

Another symptom by no means uncommon is a persistent and distressing hiccup. At times there is a constant desire to urinate and very large amounts of urine may be passed.

Diagnosis.—The differential diagnosis of angina pectoris has two objects in view. The decision, in the first place, of whether or not it is an attack of real angina or of the nervous or pseudo-angina or some allied conditions. In the second place, what is the cause that has set in motion this symptom complex? The sudden onset, the intensity of the pain, the fear of instant dissolution, the lack of dyspnea, the usual slight variation from normal in the pulse, the immobility of the patient and the pinched and drawn expression of the face, make a characteristic picture that is strongly impressed upon the mind. But these are typical cases. These attacks may occur at any age and in men and women, but they most frequently occur in men after the middle period of life, the pseudo-angina usually occurring in women, and the history of fear of heart disease and with it the fear of sudden death, is strongly marked in their minds, and they are influenced by the suggestion from having heard of, or having seen some person in an anginal attack, or by the imagination of how it would occur if it were true. One thus sees the picture varied in detail. Dyspnea, fright and convulsive twitchings and a great deal of jactitation or restlessness is more characteristic of the nervous type of false angina and is usually seen in younger men and women than those in whom one would expect to see true angina. However, there may be a true stabbing cardiac pain or precordial pain that starts the appearance of the false attack and when once it starts it may go on to terrified completion. The vasomotor symptom of flushing is more pronounced in false angina. Pallor, coldness and sometimes sweating, occur in both true and false angina. The ashy gray or livid blue is more characteristic of the true angina. Moreover, in true angina, there is an unavoidable, unsought-for conviction within that death is imminent. In pseudo-angina, one is impressed more with the fact that the patient is badly frightened. In false angina it is evident that the patient is afraid to die. In true angina it is not so much the fear of dying as it is the realization that it may not be possible to avoid death. The pain itself in false angina rarely has the agonizing quality of the pain of true angina and it seldom is accompanied by the real spontaneous feeling of impending death. Moreover, in pseudo-angina, rarely does the pain radiate down the arm, but it is more the precordial pain radiating around the heart, while only in the true angina is the pain of vise-like constriction holding the chest. Sometimes false angina is accompanied by a nervous chill. The false attacks, moreover, are preceded by flushes or feelings of oppression and they may be preceded by various nervous phenomena. In true angina the onset is almost always sudden and can be traced to some definite exertion, emotion or indiscretion of eating, while the attacks of pseudo-angina are rarely excited by effort and are more apt to occur spontaneously without sufficient cause. They may be said to occur more from emotional causes and less from physical effort than the true angina. True angina occurs at night, waking patients out of a sound sleep. False angina does not and one is justified in saying that it is a symptom complex of the hours of waking consciousness. In listening to the heart in the nervous form of anginal pain, one is more apt to hear mitral murmurs or fairly good cardiac sounds and good rhythm, or, at most, occasional extra-systoles. Both the first and second sounds over the aorta may be exaggerated. In true angina one is very apt to hear a ringing, drum-tap second aortic sound due to the fusion of the three layers of the aorta from an old aortitis or an old syphilitic involvement of the vessels. One is more apt to hear the two aortic murmurs or make out by percussion the dilatation of the aorta. One frequently hears in the subjects of true angina the fetal rhythm of evenly spaced and even value to the heart sounds of chronic myocardial brown atrophy, or the gallop rhythm of myocardial fibroid replacement. The radiation of the pain is an excellent means of differentiation between the pain of real angina and many kinds of precordial pain.

Tobacco causes precordial pain on the edge of the pectoral muscle situated usually about the nipple. Intercostal neuralgia, in which the intercostal nerve is painful and tender is often thought to be angina by those possessing it. In those who have cardiac disease, precordial pains not uncommonly come and go, but they do not take the paroxysmal form of anginal attacks. In chronic alcoholism there is often a persistent precordial pain with tenderness of the pectoral muscles. The pain of angina is, as we have already said, substernal and while its radiation may be unusual, the fact that it radiates from its point of occurrence in the chest out into the cervical and dorsal segments of the cord, is indicative of real angina. Pain following walking against the wind, or exertion, appearing in the arm rather than in the chest, relieved on cessation of effort to reappear when effort is again begun, or accompanied by globus and relieved by eructation of gas and this phenomenon repeated, *should cause one to think of real angina rather than to discard this* diagnosis. Anginal attacks following syphilitic infection or following influenza should not be considered of false character. The pain of herpes zoster cannot always be differentiated from the pain of true angina, for Neusser reports a case where herpes zoster developed in the upper extremities after an attack of real angina. This is also true where there is hyperalgesia of the skin, which has been known to be left following a case of angina. The persistency of the pain and the tenderness in the skin over more or less wide areas after a few days clear up the diagnosis even before the characteristic rash and vesicles appear. Neusser states that ''phrenic neuralgia is observed in many forms of diaphragmatic pleurisy, in pericarditis, in aortitis and dissecting aneurysms and is characterized by dyspnea, later by singultus, sensations of constriction at the insertion of the diaphragm and at the neck and frequently by the radiations of the pain to the left arm.'' Differential diagnosis would depend upon the physical signs of the pericarditis and the pleurisy and fever. It should not be forgotten, however, that true cases of angina pectoris in the early stages of pericarditis are rare, but occur, as reported by several observers. Many cases reported have been in reality instances of coronary thrombosis in which the anginal attacks have occurred and a day or two later a pericardial rub has been recognized. The anginal symptoms have been attributed to the pericarditis and not to the real cause, the coronary thrombosis.

Complications and Sequelæ.—Angina pectoris is not a disease. The symptom complex of angina may, therefore, be said to be more a complication of other diseases than to have complications of its own, and the same may be said of its sequelæ. It is a complication of coronary thrombosis or of aortitis caused by rheumatism, by influenza or by syphilis. It is a rare complication of an acute pericarditis and is sometimes a sequelæ of a former pericarditis when old adhesions pull on the origin of the aorta.

Association with Other Diseases.—Trousseau claimed that angina was associated with epilepsy, believing that there was a close relationship. Osler quotes Richardson also as comparing angina pectoris with epilepsy. Cases have been reported in which patients had both angina and epilepsy, one peculiar case being reported by Osler, in which there was a very marked aura of the epileptic, well-marked pain and the sensation of impending death, but the patient did not connect the two in any way and they were recognized in his consciousness as occurring separately.

Persons who suffer from attacks of angina pectoris may naturally acquire other diseases but there is no regular association to the attack of angina except with the groups of diseases which cause infection, with morbid changes in the aorta, coronary arteries and infections or degenerations of the myocardium. When once the foundations are laid which set in motion the reflex of the anginal complex, then disordered functions of digestion or of the kidneys may be the active agent in starting the anginal mechanism in motion.

Clinical Varieties.—True angina may well be separated, as was done by Elsner, into the large and small attacks. The large attacks arise suddenly, usually after exertion, worry or a heavy meal. In these the pain is intense with wide radiation, and the sense of impending death weighs heavily upon the patient. Probably the majority of patients seen in angina suffer from small attacks suggesting severer paroxysms or the possible development of them. These minor attacks are definitely less severe and the pain is definitely less. At times they lack the sense of impending death but at times it is present to a greater or less degree. If the morbid conditions have continued for some time, these slight attacks are apt to occur on slight cause. They are of short duration, however, and in the majority of cases cease promptly with rest. The pain rarely radiates beyond the left shoulder. It is not apt to go into the root of the neck or the throat. In one patient, the author has seen a small attack consist of a single terrific sharp shoot of pain in the great occipital nerve from the nape of the neck up to the top of the head. In these patients at times, in both the severe and minor attacks, the numbness in the arm and the inability to use it is noticeable. As long as the numbness persists, any use of the arm may bring on increase of pain or the return of an anginal paroxysm, the numbness being felt after the real attack has subsided. The substernal pain usually subsides first, the pain in the arm more slowly, and the numbness of the arm may persist for a day or more. One small attack may be the forerunner of the severest attack, but the patient may go for years with small nagging attacks before the severer ones develop.

Besides the major and minor attacks, individuals vary clinically in their manner and areas of manifesting the clinical evidences of the same pathologic lesions underlying the symptoms. There is a certain wide variation within normal limits of vascular distribution and nerve supply to the same viscera or to the different areas of the body. One spinal nerve or efferent sympathetic may in the majority of individuals go to a certain area, but in other individuals the same area may be supplied by another nerve which, when involved in the morbid process, will present quite a different clinical picture. The aortic plexus receives nerves from the upper cervical, upper and lower thoracic nerves, and their distribution on the aorta may vary, or the area involved may equally vary and produce pain in the neck or arm or downward in the back or legs, depending upon the sensory and efferent arc stimulated. In the author's experience, however, paroxysms of anginal pain from aortitis very commonly radiate the pain upward into the neck and throat and the intense constricting crushing thorax pains seem also to come with the involvement of the aorta rather than of the heart itself. The pain of aortitis is also more distinctly substernal and less commonly precordial.

When thrombosis of the coronary arteries takes place there may be intense paroxysms of anginal pain radiating in its characteristic manner down the left arm. Or there may be no pain. When the symptom complex of angina does appear in coronary thrombosis, the essential clinical peculiarities, as described by Libman, are the rapid pulse, a sudden fall of blood-pressure, a leukocytosis, and in twenty-four or thirty-six hours the appearance of a pericardial rub over the involved area of the heart. Later, if the circulation to either left or right bundle be involved, the characteristic bundle defect in the record of the electrocardiogram will show itself. Often, as the heart recovers itself, there will be present the galloping rhythm of the heart sounds which will often persist for months after the attack. In these attacks of coronary thrombosis, dyspnea, sometimes to a distressing degree, and often cyanosis with rapid pulse rate are present and the cardiac sounds are feeble. Herrick of Chicago divides these cases into four classes: Sudden death in pain; angina with death in a few minutes; non-mortal attacks with slight angina from the obstruction of a small branch; and severe forms fatal after a long period. Allbutt draws attention to the character of the anginal pain in the thrombotic cases as being in kind and intensity and in position of substernal, epigastric or submammary the same as in other forms of true angina, but the pain here is more continuous and occurs less in paroxysms.

Angina Sine Dolore.—Gairdner first described the form of the anginal complex in which real anguish of spirit and the conviction of instant death but no pain is present as *angina sine dolore.* The other accompanying symptoms of usually normal pulse, absence of dyspnea and death in one of the paroxysms were present, the attacks being analogous to the true angina, only dissimilar in their absence of pain.

PSEUDO-ANGINA.—Another variety is *pseudo-angina.* This is very apt to develop more frequently in women than in men, and in younger than in older people. Also it develops in those who have had friends or relations die of angina or of heart disease, or who, through some reason or some statement made to them because they perhaps possess a cardiac murmur, are convinced that they have heart disease (which to them means sudden death). And again it may develop in patients who have some other form of pain in the precordium. The pain in true angina is substernal near the xiphoid or up near the third rib, but in pseudo-angina it is more apt to be in the mammary line in the fold of the pectoralis major. Hyperalgesia may remain in the skin in both true and false angina. Attacks of pseudo-angina, when they come, are usually accompanied by nervous manifestations beforehand. They do not come suddenly, they do not follow physical exertion, but are apt to follow emotional strains. Patients are more apt in these attacks to have clonic convulsive spasm or develop a nervous chill. They are apt to have flushed faces while their extremities are cold, but in true angina there is more apt to be the real sweating. There is apt to be dyspnea and rapid pulse in false angina. The weak and feeble or irregular pulse belongs to the true angina. In pseudo-angina patients do not die.

TOXIC ANGINAS.—Toxic anginas are most frequently brought on by tobacco. As Osler points out, the disproportionate amount of angina pectoris in nonsmokers in ratio to those who smoke to excess is striking. There are a large number of persons in whom tobacco causes a precordial pain, but this pain does not go to the severity of an anginal attack nor does it become substernal or radiate in the usual way. Patients, however, who suffer real angina increase the number of their severe attacks by the use of tobacco. The author had one patient come to him with intense pain in the chest at the area of the third or fourth rib on the left side which did not radiate to the arm. Upon walking up stairs or up an incline, intense pain would be brought on with a sense of suffocation and a sense of tightening of the chest; there was no dyspnea but the fear of death was distinct. There were no physical signs of cardiac disease. This patient was a stout, active man about forty years of age and a great smoker of cigarettes. He was advised to cut off his cigarrettes as they seemed to be the cause of his attacks. This he did and improved greatly. He kept away from them for many months and his attacks disappeared. On going back to his tobacco his pains and attacks of suffocation returned and the patient dropped dead while walking in the street. Two other patients who had attacks of real angina were warned that the smoking of cigars increased their attacks of pain and were asked to desist. This they did and improved. On taking up their smoking again, their attacks quickly returned with fatal results. One of these patients had been practically free from his attacks for a year, the other for two or three months. The latter patient had gone salmon fishing, and had refrained from smoking until one day he insisted on doing so; but it was noticed that he dropped his half-finished cigar overboard and turned pale but said nothing regarding any pain. Shortly afterwards, while walking the few hundred yards to the club house, he dropped dead without warning. Osler reports a case in which the patient had severe pain radiating down into the left arm. There was no sense of impending death. There seemed to be no organic disease of the heart. This patient showed a distinct causal relationship between the amount of smoking and the amount of pain. He also showed a form of suffocation or choking coming on at night on which Huchard lays great stress as occurring in those suffering from tobacco angina. These attacks are also not uncommon in non-smokers. Such a patient wakes suddenly, particularly just as he has dropped off to sleep. There is a sense of inability to breathe, of choking and the patient sits up striving to obtain air. There is no pain or increased action of the heart. The larynx feels as if it were shut tight and the instant any endeavor is made to bring any air through, it seems to close entirely. This may last for a few seconds or longer and the patient gradually recovers his breath and after the spasm relaxes goes to sleep again. At times these attacks bring with them a sense of helplessness and certainty of suffocation. If the patient will sit up and hold the head back between the shoulders, with the chin tipped upwards as far as possible, remain as quiet as he can, and try to breathe slowly and quietly, he will shorten the period of the intense spasm. They are something like attacks of laryngismus stridulus, although there is not usually the crow-like whoop as in false croup.

Huchard describes eight clinical types of tobacco angina. These, however, seem to vary from attacks of true angina in three of his types to various forms of gastric and cardiac poisoning by tobacco, not truly angina pectoris, although they may be present in patients who suffer from the real anginal form. Huchard claims that one form of angina pectoris of tobacco origin often shows a vasomotor type with extreme pallor of the face and dizziness with increased tension in the pulse, tending to syncope with precordial anxiety with or without pain, cold extremities and cold sweating. Anginal attacks caused by tobacco often become very distressing both in the intensity of the pain, its radiation and the intense conviction of impending death, for these paroxysms in many instances do not differ clinically from severe angina from other causes. The attacks may be provoked equally well by exertion. However, particularly in tobacco angina, one observes the incomplete and abortive attacks consisting of dyspnea with a slight precordial anxiety or simply a substernal discomfort and a sensation of the stopping of the heart and imminent death. Harlow Brooks emphasizes the fact that in the tobacco angina the pulse is frequently arhythmic and intermittent, the neuromuscular system of the heart being evidently more commonly poisoned in this variety than in the paroxysms usually encountered. All observers agree that the toxic effects of tobacco on the cardiovascular system are evanescent and quickly disappear as soon as the use of tobacco ceases. This is true when the poisoning has been only functional, and is true in the large majority of instances. Huchard and other French clinicians claim that there is an arteriosclerosis of the aorta and coronaries produced by nicotin and if this be present the anginal attacks do not disappear on the withdrawal of the nicotin but are tenacious and disappear but slowly or may be permanent and warrant treatment with iodids. It is still a moot question whether or not nicotin does produce in man aortic arteriosclerosis extending into the coronaries. The cases usually so diagnosticated may well be of infectious origin in the aorta and rendered more severe by tobacco.

Judging from the experience in this country where tobacco is so freely used, one sees but seldom the pure organic tobacco angina of Huchard. One sees the various forms of arteriosclerosis in those who use tobacco and one sees the functional type more than the intense forms of angina. There is no question in the author's mind but that tobacco in those who have anginal attacks due to aortitis or other causes, increases both the intensity and frequency of the severe attacks. The author is convinced that he has seen a few deaths produced by tobacco in those who suffered from anginal attacks, both the painful angina and the *angina sine dolore*. The tobacco seems to add to the danger of tissues already diseased and can, of itself, produce functional poisoning which in turn causes the anginal symptom complex, the latter disappearing very quickly on the cessation of the poisoning.

ABDOMINAL ANGINA.—One distinct clinical type of angina pectoris is that in which the pain begins in the epigastrium and radiates back to the spine, or else it may begin in the epigastrium and become substernal in the middle of the sternum. Osler attributed to Leared the credit of the first description of the angina abdominalis as a well-recognized clinical variety. Heberden describes it as a deviation from the regular type, more as a variation of the symptom, but mentions it distinctly. Potain describes it as angina subdiaphragmatica; and Huchard and Neusser, as angina pseudogastralgica. All authors mention the intensity of the pain, the liability to deception in the real character of the attack and the difficulty of the diagnosis under certain circumstances. Verdon has particularly laid stress upon the form of angina in which the reflex starts from the tension produced by the distended stomach. The patients usually complain of a sense of globus, of a desire and inability to get rid of gas and complain of the flatulency as the cause of their pain. Verdon mentions many cases in which globus arose whenever exertion was made, especially after meals, but when the patient stopped and rested the gas was expelled and the pain stopped instantly, to return, however, in some patients, with the renewal of the exertion of walking. Unless relieved, the attacks may go on to the most intense pain accompanied by the reflex pouring of saliva into the mouth, by the typical pale and drawn face and sweating, by the intense feeling of weakness, and by the fear of sudden death. Verdon claims that unless the spasm in the gastric and esophageal musculature can be relieved these patients will often die, even though the attacks seem slight in their beginning. The pulse in this form of angina is usually slow and full until just at the end when the full vagal inhibition comes on.

Treatment.—One must separate the treatment of the attacks themselves of angina from the treatment of the patient between the attacks to prevent the recurrence. Many patients are instantly relieved of the pain of the attack of angina by the administration of **nitroglycerin** or of **amylnitrite,** or **sodium nitrite** as recommended by Lauder Brunton for the treatment of this symptom complex. It has been the author's experience, however, that in some patients, especially in those with low tension pulse, the nitrites may fail to give relief. One patient, an eminent physician, who, suffering intensely from an attack of angina, took nitroglycerin, declared that it increased the intensity of the pain rather than relieved it. Another physician has informed the author that in his attacks of angina pectoris the swallowing of a good mouthful of **whisky** will relieve him quicker and better than glonoin. **Aromatic ammonia** with or without **Hoffman's anodyne** and with or without 1/100 or 1/50 grain (0.00065 or .0013 gram) of nitroglycerin is often an excellent remedy to relieve the pain and spasm. In severe, prolonged and resistive attacks, inhalations of chloroform have been found valuable. **Benzyl benzoate** has been recommended but it is of questionable value. **Morphin** hypodermically is often necessary and will relieve the pain and ease the reflex which the vagus is exerting on the heart, for with it the pulse improves in force and frequency even when it has been slow and weak. Livingston recommended some years ago, hypodermic injections of **ergot,*** declaring that it relieved the pain in angina pectoris. The author has given this drug intramuscularly in several sharp attacks of angina and with excellent success. It has been successful in those cases in which the glonoin did not relieve the pain. **Atropin** is recommended to cut off the vagus irritation on the heart and is spoken of very highly by many who have tried it. Small doses of **adrenalin** have been of assistance in dilating the coronary vessels in the heart or stimulating the accelerator to overcome the vagal reflex. In the abdominal forms of angina, Verdon reports that in one patient practically moribund, he had the courage to pass the **stomach tube** into the stomach and relieved him of a mass of fluid from this viscus which brought the patient back to life and comfortable existence in a few minutes. In the severe forms of pseudo-anginal attacks, full doses of Hoffman's anodyne with ammonia and **ammoniated tincture of valerian** are very effective. This and hypodermic injections of **strychnin** and **Livingston's solution of ergot,** 20 to 30 minim (1.25 to 1.90 c.c.) doses, often prove effective. Recently, in a patient suffering from anginal pains brought about by the throbbing of an aortic aneurysm, great relief was soon obtained by doses of 5 minims

---

* Livingston's solution of ergot is made by dissolving one drachm (3.75 c.c.) of the solid extract of ergot in one ounce (30 c.c.) of sterile distilled water and filtered, then adding 3 minims (.18 c.c.) of chloroform and 3 grains (.195 gram) of chloretone. Dose, 15 to 30 minims (.92 to 1.9 c.c.) hypodermically.

(.3 c.c.) of the **tincture of aconite** to quiet the over-pounding of the heart action. This also tends to lower the rise of blood-pressure.

Between attacks the difficulty of diagnosing the source of the reflex producing the attacks influences greatly the line of treatment to be decided upon. In youthful cases arising from syphilitic infection there is no question but that the syphilis should be actively and immediately treated. The best treatment of this is some form of **arsenic** intravenously, but this should not be given in large doses but in small doses frequently repeated. For example: one-eighth or one-quarter, at most, of the usual dose of an **arsenobenzol** preparation and this repeated in five days, with a week or ten-day interval between these doses, **mercurial inunctions,** or **bichlorid of mercury,** given by hypodermic or by mouth, may be used with effect. Arsenic in many instances, in the experience of the author, has really seemed to relieve the pain of syphilitic aneurysms and of anginal attacks occurring from a syphilitic aortitis. Syphilitic lesions occurring in the blood-vessels are often stated to occur only in the tertiary stages of the disease, but this is an incorrect observation. Harlow Brooks has shown that in aortitis and myocardial involvement the syphilitic lesion occurs not only as a secondary but as an early rather than a late secondary, and the earlier the blood-vessels are treated by antisyphilitic treatment the quicker will the infection be held in check whether it be producing symptoms of angina or not. Angina due to syphilitic lesions of the blood-vessels has excellent chances of coming to complete recovery if energetically and properly treated. Rheumatic or influenzal aortitis when producing the attacks of angina pectoris should be treated as an acute aortitis or endocarditis of acute infectious origin. One of the best forms of treatment is the intramuscular or intravenous injections of **cacodylate of soda.** These should be given every day intramuscularly and every two or three days intravenously. Billings recommends from 10 to 15 grain (.65 to 1 gram) doses of this drug in a sterile salt solution and has had excellent success in subacute endocarditis. The author has used this method for many years and with success.

Some patients suffering from anginal attacks have also a high blood-pressure, one type of which shows the peculiarity of a high systolic pressure of 190 or 200 and a diastolic pressure of 80-100. This type of high pulse pressure is usually accompanied by evidences of intestinal putrefaction and can be greatly improved and controlled by proper treatment of the intestinal fermentation. If the fermentation seems to be due to the carbohydrate elements of food, the **Bulgarian lactic acid bacillus** in the form of **artificial buttermilk** taken with one half to one teaspoonful of **milk sugar** with each tumblerful of milk—which is Rettger's method of administration—will often diminish the gas and flatulency quickly. The milk sugar increases the growth of the lactic acid bacteria in the intestines and is not absorbed as quickly from the intestines as was formerly supposed. The milk sugar should be taken undissolved. If the fermentation is due to proteid, putrefaction often with excess of indican in the urine, the cultures of the **acidophilus bacillus** are more effective and this bacillus with the aid of milk sugar can be implanted in the colon and prevent the putrefaction in that region. Another method of controlling the fermentation in the intestines is to give 5 grains (.324 gram) of **salol** and 5 minims (.3 c.c.) of **castor oil** in capsules four times a day. This if persisted in for some weeks reduces greatly the putrefaction and the systolic blood-pressure comes down. If both diastolic pressure and systolic pressure are high, one must deal with the situation with a **carbohydrate diet** and low proteids, as in all probability chronic nephritic lesions are present.

Balfour in his interesting book on the Senile Heart, in dealing with the treatment of those suffering from angina pectoris, recommends the value of a **dry diet** rather than a fluid one and, in fact, recommends restricting the patient to four or five glasses of fluid a day, and this taking into account the small amount of tea and coffee allowed. His four important rules are as follows: "(1) There must never be less than five hours between each meal. (2) No solid food ever to be eaten between meals. (3) All those with weak hearts should have their principal meal in the middle of the day. (4) All those with weak hearts should take their meal as dry as possible."

In keeping the meals as dry as possible Balfour limits the fluids to about 15 ounces a day. If thirst be complained of, 8 ounces of **hot water** may be sipped four hours after each meal or only after the principal meal. This, he believes, helps clear the stomach and does not increase the amount of fluids in circulation. Hot water quenches thirst quicker than cold. Small pieces of **ice** chewed or sucked are sometimes useful, but the water from the melting ice should not be swallowed because it is apt to nauseate if swallowed. Thirst depends in a measure upon the dryness of the pharynx and sometimes a little **lemon juice** relieves it when water does not. The following dietary is recommended: For breakfast, at about 8:30, one small slice of dry toast with butter, 1 soft-boiled or poached egg. Balfour allows a little fish of short fiber, *i. e.*, haddock rather than cod, with from 3 to 4 ounces (90 to 120 c.c.) of coffee with cream and sugar or this may be replaced by an infusion of coca nibs or cream and hot water or cream and seltzer. If oatmeal with cream is desired, not more than 4 or 5 ounces of the porridge should be taken, and this should be taken alone and not followed by tea, toast and fish. The principal meal of the day should be in the middle of the day, and may consist of fish or meat, or fish and pudding, or meat and pudding. Soup, pastries, pickles and cheese are absolutely forbidden. If fish is eaten, it should never be fried, but broiled, steamed or boiled. The meats allowed are chicken, sweet breads or mutton. Vegetables are limited to a single potato, a little spinach or string beans. The desserts allowed are such as custards or simple milk puddings, such as rice or custard puddings. Ripe fruits can be taken and during the meal four or five ounces of hot water may be sipped if desired. Tea, four or five hours after the meal, may be allowed but no solid food of any kind, such as cake, crackers, bread or toast, is allowed. Hot water with Liebig's extract can be taken as substitute for the tea. Supper must always be a light meal and be taken about 7 o'clock. A little fish and potato or toast with butter or some plain pudding or bread and milk compose the meal. At bed-time, 4 or 5 ounces of hot water are allowed.

Patients who are liable to attacks of angina and who are suffering from arteriosclerosis may often go along for many years in comfort, provided that they lead a careful and abstemious life in the matter of eating and smoking. They are, however, balancing on a very unstable equilibrium and a single indiscretion may bring on an attack and the patient may die in a so-called attack of acute indigestion. Many patients learn to avoid the foods which disturb them and make them flatulent. They learn to lead a life in which they cannot hurry for trains, they cannot walk against cold winds, and find it extremely difficult to walk up steady and long grades. It is very noticeable among these patients that if they start out quickly when going to walk, their pleasure is soon spoiled by the nagging pain, but if they begin slowly the heart accommodates itself and many of them can go on for even long walks which give them excellent exercise and keep them in good condition. Damaged hearts should be made to do as much as their muscles will permit without exhaustion and steadily trained to remain in as good condition as carefully graded exercise will produce. Persons given to angina must avoid excessive emotions. They cannot afford the luxury of losing their temper but must perforce cultivate a stoical equanimity. Hunter, who was irascible, declared that he was at the mercy of anyone who made him lose his temper and, as a matter of fact, died from a paroxysm of angina induced by a fit of anger.

A drug very highly recommended in the treatment of angina is **potassium iodid**; it is recommended by Huchard, Osler and others in all forms of arteriosclerosis, whether of syphilitic origin or not. This is best given in small doses over long periods, that is, 5 grain (.324 gram) doses 3 times a day. Osler gives from 10 to 15 grains (.65 to .972 gram) a day, and if this amount does not agree he cuts it down to a smaller amount. Iodid of potassium is the form usually used, but the **iodin sodium** may be used if the potassium salt disagrees. Huchard believes that this drug should be taken from three to four years in daily doses of 15 to 45 grains (1 to 3 grams), until all signs of angina have disappeared for many months, and he believes that definite and permanent recovery is not obtainable except after many years of treatment. The vigorous middle-aged patients are the ones who stand this form of treatment best. Older patients improve more if their general hygiene, their intestines and gastric digestion are carefully watched. If the blood-pressure continues high, nitroglycerin in 1/100 grain (.00065 gram) doses 3 times a day is usually sufficient to assist the circulation to good equilibrium for the work that it has to do. In prescribing this drug, however, 1 per cent. solution is more reliable than the tablets and this should not be forgotten. In some patients **nitrite of soda**, in 2, 3 or 5 grain (.130, .195, or .324 gram) doses seems to hold its effect longer than the nitroglycerin. Many physicians believe that **digitalis** should be tabooed in the treatment of angina pectoris because of its supposed action in raising blood-pressure. Recent investigations, however, all point to the inaccuracy of this belief. Patients who show edema and failing circulation and who, on exertion, have distinct anginal pains, may greatly improve under digitalis. Huge doses to the limit that one can calculate per body weight of patient are not indicated, but those doses which will add to the tone of the cardiac muscle in the sense of increasing its systolic energy as shown in the increasing vigor of the pulse are best. One may give from 5 to 10 drops of the tincture, morning and night, or three times a day. The best preparation for long-continued use is the powdered leaves in half-grain (.0324 gram) doses made in pill form with extract of **gentian** and given morning and evening over long periods of time. The so-called adrenal residue of Rogers and Beebe, which is a residue remaining in the filtrate after the proteins of the adrenal gland have been precipitated, contains a small amount of **epinephrin.** As prepared, it comes as a black powder, and half a grain (.0324 gram) of this powder mixed with equal parts of sugar of milk in a one-grain capsule every four to six hours will often relieve the nagging anginal pains. In one patient under the author's care during a period of three years, it relieved the pains and greatly reduced the number and the severity of the anginal attacks. The patient was an elderly woman whose health was slowly failing from an ever-increasing arteriosclerosis. This preparation has made many patients comfortable who were suffering from the nagging and painful minor attacks, and it has relieved also the severity of the intense attacks.

Patients liable to attacks of angina should not go around without their remedies which they have found of use to alleviate the attacks. That is, they can mix the amount of water and aromatic ammonia and carry it in a bottle so that it can be poured out instantly and swallowed, or they can carry a small bottle of whisky if this gives them relief, their amylnitrite pearls or their tablets or solution of nitroglycerin. Patients liable to real angina have to learn to do things quietly and to be temperate in all things.

Prognosis.—The prognosis of angina pectoris must necessarily depend upon what is considered the decisive factor in bringing about the symptom complex which we know as angina. In general, the prognosis is in ratio to the severity and frequency of the attacks. A mild attack does not necessarily mean a good prognosis, because a mild attack treated with indifference may quickly be the precursor of a severe or even fatal attack. Angina of syphilitic origin is amenable to treatment and the prognosis is better than in any other form. The prognosis of angina due to influenza is good if the patient has the resiliency of youth to assist him to overcome it. The prognosis in older people suffering from the influenza angina should be guarded. The author has seen 3 patients over sixty years of age who were suffering from angina following an attack of influenza recover from angina pectoris in the last year, but the prognosis in influenzal infection increases in somberness of its outlook in ratio to the age of the patient. Pseudo-angina has a good prognosis, but the difficulty often arises in differentiating between the true and so-called false angina. Elsner says of abdominal angina that life may be materially prolonged in most cases, the prognosis depending upon the general arteriosclerosis. In cases of angina with aneurysm and aortic disease, Elsner gives an absolutely bad prognosis. Angina from thrombosis of the coronary arteries is a frequent cause of death; it cannot be influenced by any known treatment and the prognosis depends upon conditions which cannot be calculated. The prognosis of all conditions showing the anginal symptom complex is unfavorable in ratio to the ease in which the attack is produced by seemingly insignificant causes. Elsner also says that it is unfavorable in cases of marked arteriosclerosis, with marked hereditary tendencies, with carelessness of the patient, with unfavorable social conditions, failure to rest and the metabolic faults of gout, diabetes, lead-poisoning and with pneumonia. Balfour states that the less abnormal ties one can find in the heart, the more unfavorable the prognosis after angina has developed.

The prognosis of tobacco angina in the milder functional cases, even if there is intense pain with radiation is excellent if tobacco is cut off. If in the severe attacks of angina, tobacco is continued, it increases the seriousness of the prognosis. Tobacco added to the causative factors of a severe type of angina is a deadly combination.

Pathology.—Angina pectoris is not a disease in itself and has not a characteristic pathology. The most common lesion found in those dying from angina is an aortitis of the first portion of the ascending aorta, due either to rheumatism, or influenza, and most commonly to syphilis. This aortitis has usually extended into the coronary arteries. These arteries have usually been credited with being the primary lesion, but many postmortem reports mention the aortitis with healthy coronaries, and when the coronaries are involved at their origin the adjacent aorta is also implicated in the same morbid process. Other cases have shown healthy myocardium, normal coronary arteries and, at times only, an aortitis, but in some instances even this lesion has been lacking. Other hearts have been found with a thrombosis or embolism of its arteries with or without a softening in the muscles fed by the coronary branch, and here again without an aortitis being present. Other postmortems have shown normal vessels and normal hearts but with old pericardial adhesions around the root of the aorta. An inflamed condition of the connective tissue of the aorta involving the cardiac plexuses has been found in a few patients dying of angina pectoris. Neusser reports tumors on the vagus and phrenic nerves with normal hearts and arteries in a patient dying from a terrific anginal attack. In the cases of abdominal angina the aorta and its branches have been found in a marked condition of arteriosclerosis. It is evident then that there is no single lesion which is always found. It is equally evident that each lesion to which we have attributed causal relations to the anginal attacks is also found in those who have not suffered in life from the anginal paroxysm. The aortitis is the most frequently present of the lesions, but the definite factor common to all the different lesions which sets in motion the paroxysm with its fatal vagal inhibition seems at present to be the perversion of the normal functions of the vegetative nervous system expressed in terms of pain and excessive inhibition. But without question we are justified in believing that the disease of the coronary arteries, even though it is not the cause of the reflex that sets the anginal attack in motion, may well be the deciding factor in the fatal issue. We are dealing with factors occurring only during the life of the organism in the reflex actions of the vegetative nervous system, and these do not leave behind them after death traces that to-day can be recognized. They exhibit their force and effect in the perversion of function, but their examination postmortem at present is like looking at the empty, burnt-out shells of last night's fire works.

Historical Summary.—Angina pectoris was first accurately described by Heberden on July 21, 1768, when he read a paper before the Royal College of Physicians on "Some Account of a Disorder of the Breast." Previous to that, both Hoffman and Morgagni had reported individual cases in their descriptions of different kinds of dyspnea but did not separate the peculiar form of angina pectoris as was done by Heberden. In France, Rougnon, on February 23, 1768, five months previous to Heberden's description, in a letter to Lorry, described the death of Monsieur Charles, Captain of Cavalry. Most French authors claim this to be the first description of angina pectoris. Huchard, quoting Rougnon's letter, does not use any expression which described pain as a symptom in the attacks in question. Osler, on the other hand, who had evidently seen a copy of the original letter, quotes several sentences showing that the feeling of suffocation felt by the patient was associated with pain of great intensity and believes that the suddenness of the attack, the pain in the region of the heart, the abrupt termination and mode of death following exertion after a full meal, favor the decision that it was a case of true angina. Gairdner quotes the philosopher Seneca as evidently suffering from this disease, although there is a dispute as to the meaning of Seneca's words. There is no question but that Heberden's description was the first connected description of the symptom complex of angina pectoris, picturing it as a disease. In his description he notes the intensity of the pain, the apparent undisturbed serenity of the pulse, the lack of dyspnea separating it from the cardiac asthma, and the frequent fatal termination. Heberden did not separate the pain from the anguish and fear of death. Latham seems to have been the first to have differentiated the two symptoms. Heberden believed it was a disease due to spasm and that the heart was not involved except late as a part of the fatal termination. Jenner was the first to describe the association of the disease of the coronary arteries with angina pectoris. This was done in a letter to Heberden in 1776, after Jenner had seen the famous John Hunter, who had had his first attack of angina pectoris in 1773, and his second in 1776. Jenner did not publish his letter, as he did not wish that Hunter should know and see his opinion. Hunter suffered for twenty years from angina pectoris and, as is well known, died at a meeting of the Hospital Board of the

St. John's Hospital in October, 1793. Further descriptions of the disease were published by Frothergill, Parry, P. M. Latham, Stokes and other English physicians. Allan Burns, in 1809, was the first to bring forth the theory of intermittent claudication, and John Latham, in 1812, described a form of angina which he called *angina notha,* or false angina. The term pseudo-angina, according to Huchard, was not introduced until 1846, by Lartigue. Lauder Brunton was the first to suggest the treatment of the vascular spasm with the nitrites. Leared was the first to describe abdominal angina and Gairdner first applied the name of *angina sine dolore* to the painless attacks of the angina symptoms. Huchard collected sixty-four different opinions from many well-known physicians as to the cause of angina pectoris. Rougnon and Heberden believed in a spasm of the heart. This was to differentiate it from inflammations. Hunter and Jenner believed it to be due to ossification of the coronary arteries. Parry considered it as a spasmodic condition of the myocardium, a momentary exaggeration of an existing feebleness of the heart. Frothergill thought it to be due to fat in the mediastinum. Stokes explained it as due to a dilatation or obstruction of the right ventricle following a paralysis or weakness of the left ventricle. P. M. Latham considered angina as not a disease entity but a symptom complex. Grinza, Corrigan and Lancereaux believed it to be due to a lesion of the aorta, as aortitis, dilatation, or aneurysms, pressing on the cardiac plexus. Virchow, Cohnheim and Quain believed it to be due to embolism or thrombosis of the coronaries. Contraction or obliteration of the coronaries was supported by Kreysig, Parry, Potain, See, Huchard, etc. Various combinations of spasm, intermittent claudication and atheroma of the coronary arteries have been given to explain the symptom complex of angina, especially by Huchard. Others, like Bouillaud and Bucqury, have claimed that there were two sorts of angina pectoris, one coronary and the other neuralgic or neuritic. Desportes describes it as a neuralgia of the pneumogastric plexus with extensions to the gastric and pulmonary and cardiac plexuses and of morbid processes of the organs to which these plexuses are distributed. Laennac believed it was due to pulmonary and cardiac neuralgias forming two kinds of anginas. Various other neuralgias, neuritis of the cardiac nerves, cardiac ganglia or of the cardiac plexuses have been held to be the cause by different authors at different times. Trousseau believed that angina pectoris was a manifestation of epilepsy. Others have thought that it was due to manifestations of gout in the heart or gout in the aorta or some gouty manifestations of the diaphragm. Others have expressed it as a rheumatic affection of the aorta or the cardiac plexuses. Sir James Mackenzie in his latest writings believes it is due to an exhaustion of the cardiac muscle. In other parts of the same article, he speaks of it as if it were of nervous or vascular origin. Sir Clifford Allbutt believes that it is due to an aortitis except when it occurs as a symptom complex of thrombosis of the coronary arteries. Verdon, on the other hand, believes it to be a neurosis of the various segments of the cord in which the neurons show evidence of inflammatory processes. Von Neusser, of the Vienna school, following Bamberger, his former chief, believes it is a nervous reflex as the expression of some stimulus exerting its force somewhere in the nervous reflex arc of afferent and efferent nerves which finally find their expression in the vagus reflex.

This short historical review is sufficient to show that from Heberden's time to the present the etiology and pathology of this symptom complex are still matters of opinion and not of demonstration. The diagnosis, the clinical description and the treatment are matters of general agreement in the profession. The etiology and pathology are still matters of general dispute.

CHAPTER VI

INSTRUMENTS OF PRECISION IN CARDIOVASCULAR STUDIES

BY ALEXANDER LAMBERT, M.D.

Historical, p. 281.
Instruments, p. 289.—Stethoscope, p. 289; Phonendoscope, p. 291; Sphygmograph and Electrocardiograph, p. 291.
Physiology of the cardiac cycle, p. 294.
Cardiographic curves, p. 295.—Methods of taking tracings, p. 299; Reading of tracings, p. 300; Measuring of tracings, p. 303; Significance of various curves, p. 304.
Cardiac arrhythmias, p. 305.—Auricular irregularities, p. 305; Heart block, p. 308; Ventricular ectopic beats, p. 309; Pulsus alternans, p. 309.
Crehore micrographic curves, p. 309.
Jacquet curves, p. 310.
Electrocardiograms, p. 312.—Method of making electrocardiograms, p. 313; Interpreting electrocardiograms, p. 313.
Curves taken with the optical capsule of Franck, p. 318.

Historical.—A discussion of instruments and their clinical value cannot be treated on the basis of a definite scheme of procedure as etiology, pathology, symptoms, etc., but must be reversed and developed from a historical basis in their relation to the medical ideas of their period and in what manner each instrument advanced medical knowledge and clinical precision by its use. The term "heart disease" must also be made equivalent to "disease of the heart and circulation," for increased medical knowledge has come at times through concentration of study on the heart itself, as when Laennec developed the stethoscope; and at other times through study of the peripheral circulation, as when a few years ago MacKenzie and Wenkenbach focused medical attention on the peripheral circulation and showed what increased knowledge of cardiac irregularities could be obtained by an accurate comparison of the venous and arterial circulations. Many writers, the English especially, have rightly deprecated the present separation in medical literature of the diseases of the heart itself from those of the blood vessels. This separation followed as a reaction against the barren study of the pulse in the 18th century and as a logical sequence in the 19th century from the exclusive concentration of medical attention on the cardiac valvular defects in the study of circulatory diseases.

Aristotle knew of the "leaping point" in the fourth day embryo of the chick and held the doctrine of the primacy of the heart and that the first to be generated was the last to die. An older Greek doctrine held to the primacy of the blood. But even though the heart could be seen to pulsate in the embryo and felt to pulsate in the body during life, the post-mortem emptiness of the arteries was held to be the deciding evidence that the arteries contained air or spirits and only the veins held blood during life.

The ancients, however, with the exception of Herophilus of Alexandria, apparently did not use instruments of precision in the study of circulatory diseases to aid them clinically. This physician used a clepsydra or water-clock to time the pulse, and appreciated the significance of pulse variations in their relations to the general condition of the body. Hippocrates, though such an accurate observer, does not once allude to the pulse in his "Aphorisms and Prognostics." The term *σφυγμος* he used in the sense of a preternatural throbbing or beating, and not in that in which it was subsequently employed. The real value of pulse rate and its ratio to respiration and temperature is relatively a modern conception, and the ancient medical doctrines centered around the blood as a source of the innate heat of the body and its ardent spirits and clinically on the various organic pulses as taught by Galen, a different pulse for each disease of each organ and the diagnostic meaning and prognostic significance of pulses fast and slow, large and small, frequent and infrequent, regular and irregular. Galen at times laid as great stress on the pauses between pulse beats as on the beats themselves. Galen was the first to show and teach that the arteries during life contained blood, and he knew of the heart beat and its valves, but his ideas of vital spirits in the blood and its humors led him astray, and he was carried away more by his philosophic theories and controversial ardor than led by facts to believe that the veins sprang from the liver and the arteries from the heart, and that the blood surged through the body by a tidal ebb and flow, passing by unseen passages in the cardiac septum from right to left ventricles.

Autocratic rule kept state and society together in the western world and authoritative statement governed man's thoughts in medicine as in other fields from Galen's time until the Renaissance; hence, Galen's ideas dominated medicine for over a thousand years.

Leonardo da Vinci in the last half of the 15th century made remarkably accurate drawings of the heart, described the coronary arteries and their function, and stated that by the contraction of the heart the blood is driven into the arteries; but his manuscripts remaining unpublished and left hidden in mirror writing, he made no impression on the medical ideas of his time.

Vesalius a hundred years later (1543) rebelled against tradition and published his human anatomy based on observations and facts, and laid the foundations for accurate anatomical knowledge and the disproof of Galen's cardiac and circulatory fallacies. He strongly questioned the permeability of the septum but retained the Galenic theory of the venous and arterial circulations and their tidal ebb and flow.

Michael Servetus in his youth fleeing from the Spanish Inquisition studied medicine in Paris and was prosector of anatomy with Vesalius. By 1546 he had written in manuscript his book "De Restitutione Christ ianismi," which was published in 1553, in which he described accurately the circulation of the blood from the right heart through the pulmonary artery to and through the lungs and to the left heart by the pulmonary veins. He also described the mixture of the inspired air and blood as well as the change of color of the blood from that in the right side to its crimson color in the left ventricle. Servetus in this book differing so widely from the orthodox anatomy of his time, differed equally so from all orthodox theology and was burned at the stake by Calvin in Geneva in 1553.

Fabricius, a successor to Vesalius, at Padua in 1574 published illustrations and described the valves of the veins, but being a strict Galenist he failed to appreciate their meaning and draw the evident deduction of venous flow in only one direction. Andreas Caesalpinus in 1593 in his "Quaestiones Medicae" seems to grasp the fact "that from the vena cava a flow takes place into the right ventricle, whence the way is open into the lungs. From the lungs, moreover, there is another entrance into the left ventricle, from which then a way is open into the aorta artery, certain membranes being so placed at the mouths of the vessels that they prevent return. There is a kind of perpetual movement through the heart and lungs into the aorta artery." He also drew attention to the fact that when a vein is ligatured it swells on the far side, which would be impossible if the Galenic tidal flow from the heart through the veins took place. But Caesalpinus failed to put it all together.

Thus was the foundation laid for William Harvey, who between 1597 and 1601 studied medicine in Padua under Fabricius and was familiar with the learning of the Italian School. Returning to England in 1602, in 1616 as Lumleian Lecturer he announced his investigations on the circulation and gave his conclusions, viz., a complete circulation of the blood from arteries to veins through peripheral porosities and back to the heart again through the veins and from the right side of the heart through the lungs to the left heart, the heart itself containing an impermeable septum. These were not published until 1628 in his "De Motu Cordis." Harvey upset the beliefs of two tidal circulations, a venous and arterial, and also that only a portion of the blood went into the right heart to the lungs, and that the arteries received nourishment and the veins spirit. He also was the first to substitute the systolic contraction of the heart as the propulsive force to drive the circulation, in place of the diastolic sucking power to draw the blood onward in the arteries. Later in life Harvey also proved by experiment the impermeability of the cardiac septum. Harvey could not bring himself to believe that the blood received anything from the air during its circulation through the lungs. He thus failed to solve the urgent question of his time, "cui bono," for what purpose, was the circulation and why was all the blood sent through lungs. He was a true follower of Aristotle and tried to explain the necessity of the circulation as due to the innate heat of the blood which is celestial in nature and identical with the essence of the stars, and harked back to the Greek doctrine, older than Aristotle, of the primacy of the blood as being generated before the heart. Four years after his death Malpighi proved by the miscroscope the capillary circulation in the mesentery of the frog, and thus closed the gap left by Harvey and explained what Harvey's peripheral "porosities" were and how in the peripheral capillaries the arteries and veins joined. In 1674 John Mahow published his proof of the absorption of air by the blood in the lungs and the purpose of respiration, and answered the "cui bono" of the circulation, the contention of Harvey's times. Mahow also finally discredited the ancient idea that the heart was for the cooling of the blood and ardent spirits.

Harvey's work was done without instruments of precision. Experimentation and observation without such aid was baffling, as Harvey describes.

"When I first gave my mind to vivisections as a means of discovering the motions and uses of the heart and sought to discover these from actual inspection and not from writings of others, I found the task so truly arduous, so full of difficulties, that I was almost tempted to think with Fracastonius that the motion of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place nor when and where dilatation and contraction occurred, by reason of the rapidity of the motion, which in many animals is accomplished in the twinkling of an eye, coming and going like a flash of lightning. So that the systole presented itself now from this point, now from that, the diastole the same; and then everything was reversed, the motions occurring as it seemed variously and confusedly together; my mind was therefore greatly unsettled, nor did I know what I should myself conclude nor what believe from others."

The late Dr. S. Weir Mitchell states that Herman Kepler, the astronomer, was the first to count the pulse or at least the first who before 1600 has left a record of having done so. Herophilus must have counted it to time it, but no physician seems to have left a record of it previous to this time. Kepler used the pulse as a measure of time, contrasting the mind's ability to appreciate this small measure of time with its inability through the eye without the aid of instruments to measure curves or motion at a distance: "For a moment, it may be one second, the smallest division of an hour, which generally is equal to the pulsation of the arteries, is a perceptible time"; and Kepler further says in 1618 that in a healthy man "generally for each second there is a pulsation of the artery with no discrimination between systole and diastole. Thus there would be in one minute sixty pulsations, but this is rare; commonly seventy can be counted; and in the full-blooded and in women eighty, four to each three seconds; briefly, in one hour four thousand or less." Mitchell adds, the clock with which Kepler counted the pulse must have been a balance clock such as his master Tycho Brahe used.

Galileo when an eighteen year old medical student used his pulse to prove that the large bronze lamp swinging in the Duomo at Pisa swung to either side of the center in equal time. Forty years later he judged the accuracy of his first clock by the measure that it would not vary by so much as the beat of a pulse. The reversed idea suggested itself to the young medical student and he constructed such an instrument to measure the pulse by a pendulum. This Viviani says was hailed with delight and much used by the physicians of his day. Galileo never claimed this and it was attributed to Paolo Sarpi. It was later taken up by Sanctorius, who, like Galileo, called it a pulsilogon. In his Commentaria, published in Venice in 1625, Sanctorius says he has contrived four instruments: "The first is my pulsilogon, by which with mathematical certainty and not by conjecture I can measure the variation and degrees of the pulse both as to frequency and as to slowness. It is composed of a little cord made of linen or silk, to which, as may be seen, is fastened a leaden bullet, which being struck if the cord be long the motion of the bullet will be slow, and if the cord be short the motion will be quicker and more frequent." This bullet struck by the finger swung before a marked scale and a white mark on the bullet aided the ease of observation.

Although watches had been invented, it is said in Nuremberg, at the end of the 15th century, they were not in general use nor had it occurred even to Harvey to use the frequency of the pulse clinically, for in all Harvey's works the number of beats is spoken of but once as being from 1,000 to 4,000 in half an hour.

Although the watch "even as it is today may be called an 18th century invention," in the last years of the 17th century Daniel Quare put on watches the minute hand, which Sir John Floyer called a middle finger, and in 1707 invented and described a pulse watch which ran sixty seconds. In the preface of his book he says: "I have for many years tried pulses by the minute in common watches and pendulum clocks, and then used the sea minute glass which was employed to test the log." Even these observations made but little impression on medical thought. In the 18th century the clinical observations on the circulation went wildly astray following the doctrine of specific pulses, a pulse for every malady. Mitchell designates it as "observation gone minutely mad . . . an exasperating waste of human intelligence. . . . I know of few more dreary deserts in medical literature." De Haen put these doctrines to clinical test in Vienna and rejected them, and this discouraged the spread of the doctrine, but it survived well into the 19th century. The French, Spanish, and Italian schools accepted it completely, and Bordeu sneers at Floyer's work, while Fouquet thought all pulse enumeration useless curiosity and sphygmometric instruments idle toys. Falconer in 1796 says that Floyer's methods were unused until then. Neither Heberden nor Falconer made much impression on their contemporaries. Even Rush and Cullen pay little attention to counting the pulse and respiration. Mitchell also stresses the fact that in Corvisart on the Heart and in all the pages of Laennec there is but one pulse count and no enumeration of the breathing. As late as 1833 in the Dublin Medical Journal we find the criticism of Heberden's paper that while it contained some useful remarks it has been productive of injury, as he reduced all observations of the pulse to its frequency as that can be so exactly measured by a watch.

Formey in Berlin in 1823 and Nick's "Studies of the Pulse," published in Tubingen in 1826, emphasized the real changes of the pulse in health and disease. But, as Mitchell says, it was not until the influence of the great Dublin school made itself felt that the familiar figure of the doctor, watch in hand, came to be commonplace.

The accurate knowledge of the circulation and heart was advancing through the physiologists, even during the clinically dreary years of the 18th century. Harvey's discovery had greatly stimulated the physiologic investigations. Stenson in 1664 published his accurate observations on the contractions of muscle, and Barelli, Malpighi's colleague, laid the foundation for the neurogenic theory of cardiac contractions when he discarded the ancient animal spirits and brought forward the idea that his succus nerveus passed from the nerves into the muscles, starting a fermentation which caused the contraction with an actual increase in the muscle.

Francis Glisson in 1672 refuted the false notions of muscular contraction as due to animal spirits or the succus nerveus, and proved by his plethysmograph that muscle when contracted does not increase in volume. He wrongly thought muscle diminished in volume but was correct in his opinion that the individual fibers became shorter.

In 1728 Lancisi (De Motu Cordis and Aneurysmatibus) describes the undulation of the cervical veins, which Flint notes as of great interest in view of our present day use of the polygraph. Stephen Hales, rector of Teddington, in 1733 laid the foundation of blood-pressure determination by his manometer experiments. Albrecht von Haller, who further elaborated Glisson's theory of muscle irritability, proved that irritability is a specific property of muscle and different from the irritability of the nerve which vis nervosa came to the nerve from the brain. He applied this function of irritability to the heart muscle and thus founded the myogenic theory of cardiac contraction. Haller was so far in advance of his times that many later discoveries have been rediscoveries of his forgotten works.

Poiseuille in 1828 improved on the straight manometer of Hales by substituting a U-shaped tube containing mercury. This connected with the artery by rubber tubing filled with sodium bicarbonate solution prevented blood coagulation. This instrument in 1847 was improved by Carl Ludwig, who added a float with pen attachment to write on a recording cylinder. Ludwig's genius thus made possible comparable records measured by time and space. In Ludwig's laboratory the modern work on the problems of the circulation steadily developed and the advances of modern physiology have continued. But the record of these achievements belongs to physiology and although they are the foundation of our clinical knowledge we are more concerned here with instruments in everyday clinical use.

A clinical discovery and an instrument of equal value in their far-reaching influence in medicine were given to the medical world in the early years of the 19th century. Leopold Auenbrugger of Vienna published in 1761, aften seven years of research, his book "A New Invention for Discovering Obscure Thoracic Diseases by Percussion of the Chest." This work went unnoticed for forty years. Even De Haen working practically alongside of Auenbrugger failed to grasp the value and meaning of this work. Corvisart giving all the credit to Auenbrugger republished the book in 1811. Corvisart, Napoleon's physician, holding the chair of clinical medicine in Paris, had the widest audience of his time, and his enthusiastic acceptance and application of this new method of percussion spread the knowledge of it broadcast in Europe and its inherent clinical value enforced its general acceptance.

Laennec's stethoscope was the instrument which came so opportunely to supplement percussion. This was discovered by accident, being at first but a roll of paper applied to the precordial region that the ear might avoid touching an unusually dirty patient. The cardiac sounds were heard so much more distinctly that Laennec's genius immediately appreciated his opportunity, and the monaural stethoscope resulted. His original instrument was a wooden tube about six inches long, the hole in its center being three lines or a quarter of an inch in diameter.

Although Laennec's interpretation of the pulmonary sounds are still accepted as true, his interpretation of the cardiac sounds was not as correct. But even then it has been given to but few men to advance the clinical knowledge and revolutionize the ideas of his time as did Laennec in his short life.

Morgagni had described the different valvular diseases and the resulting cardiac changes of form found post mortem, and Senac and Corvisart, Laennec's immediate predecessors, based all their clinical deductions on pathologic findings. But with the stethoscope the circulatory functions, during life, of the damaged heart could be observed. Brouillard, James Hope, Adams, and others, accurately defined the meaning of the cardiac sounds and murmurs. During the 19th century, however, the general knowledge of the medical profession remained almost entirely focused on valvular diseases and endocarditis; only towards the later years of the century were diseases of the myocardium generally appreciated. Medical teaching during these years generally separated diseases of the heart from those of the blood-vessels, and in considering the breakdown of circulatory equilibrium the heart in most medical minds was divorced from the rest of the circulation. A study of the pulse, however, was still persisted in by a few, and Marey in 1857–60 invented the wrist sphygmograph. Bamberger and Marey graphically recorded the movements of the jugular vein in 1863, and Potain in 1867 still further added to the knowledge of both arterial and venous graphic curves. Von Frey improved on the lever of Marey's instrument and Dudgeon made the instrument more compact and replaced the simple with a compound lever, which writes without an arc on a horizontal surface. Jacquet improved the instrument by a firmer support on the wrist and by adding a time marker. Frank and Petter (1908) replaced the flat spring on which the button, resting on the radial artery, works by the action of a spiral spring and lever. The tension of the spiral spring is also regulated by screws. Jacquet (1910) revised his instrument, using the spring and lever but retaining the fixed bearings of his marking levers. MacKenzie modified the Dudgeon sphygmograph and added a time marker so that he could compare tracings simultaneously taken from the right jugular and the carotid or radial artery or apex beat. This he called the polygraph.

MacKenzie succeeded in solving the riddle of the cardiac arrhythmias by comparing the orderly sequence of events in the cardiac cycle as they occurred synchronously on the right and left sides of the heart. He published his first papers in 1893–4 and in 1902 his book on "The Pulse." Fortunately during these years Stanley Kent (1893) and His, Jr. (1893), first described the auriculo-ventricular bundle, and Tawara, working under Aschoff (1906) described accurately and in great detail the auricular ventricular node and the bundle with its two branches going one to each ventricle. Keith and Flack (1907) added to this knowledge the location of the sino-auricular node. A comprehension of the pacemaker of the heart and the conducting system of its impulse was thus made possible. The polygraph showed the orderly sequence of contraction of auricle to ventricle and the time of transmission of the impulse between chambers. It also showed delay or blocking off entirely of the impulse in its passage down the bundle between auricles and ventricles. The polygraph also showed clearly the occurrence of the ectopic beats and that these beats arose in auricles or ventricles or in the nodal tissue between. But it left certain arrhythmias unsolved, such as auricular fibrillation, showing in this frequently occurring clinical condition an absence of the wave of auricular contraction but giving no clue which might lead to the true solution of the problems involved.

In 1901 William Einthoven of Leyden brought out his electrocardiograph. Waller in 1889 had shown that there was a measurable difference of electromotor potential arising in the heart just prior to its contraction. Einthoven in his electrocardiograph measured this difference of electric potential by passing the current through a tiny platinum or silver-plated glass string suspended between the poles of an electromagnet. The string vibrated at right angles to the currents in the magnet and these vibrations, magnified by lenses and reflected by an electric light, cast a shadow on a moving film or plate in the slit of a camera. The curves thus obtained show characteristic forms for stimuli starting normally in the sino-auricular node giving an auricular contraction, and passing normally down the bundle of His to each ventricle. The curves also show any delay in the passage of the stimulus from auricle to ventricle, any failure to pass from auricle to ventricle or blocking in passage down either branch of the bundle, and further show the origin of ectopic beats whether of auricular, nodal, or right or left ventricular origin. This instrument solved the problems of the tachycardias and auricular fibrillation and showed the existence of auricular flutter.

To Thomas Lewis and his co-workers in England is due the credit not only of being pioneers in the solution of the clinical value of the electrocardiograph and of demonstrating its practical value to the profession as Mackenzie has done for the polygraph, but also of solving by means of this instrument the intricate question of the normal and abnormal transmission of the cardiac impulse. Erlanger, Meek, Eyster, Cohn, Hirschfelder, and others in this country have further developed our knowledge of the clinical meaning of the electrocardiogram.

Before the full value of the electrocardiograph was appreciated it was thought that further perfection of sphygmographic instruments would give information regarding the cardiac mechanism which the clinical polygraph failed to show. Wiggers showed that all these sphygmographic instruments have certain inertia defects inherent in their construction and the materials of which they are made. To overcome this, Francois Franck invented his optical capsules, which by a mirror fastened to the rubber tambour reflect the oscillations of the tambour by means of a beam of light from a Nernst lamp on to a photographic film revolving in a camera. This reduces the instrumental errors to a minimum. Another instrument which also eliminates the instrumental errors is Crehore's micrograph which transmits the venous and arterial waves by means of the air column in the usual rubber tube but instead of the open-mouthed funnel ordinarily used over the jugular or apex a metal tambour is used with a rubber membrane stretched over the open face. This gives a closed tambour transmitting the vibrations through the rubber tube to a closed air chamber under a diaphragm, similar to a telephone diaphragm, on the upper surface of which is fastened a mirror. Just above this mirror and parallel to it is a cylindrical plano-convex lens with its plane surface towards the mirror. The movements of the mirror on the diaphragm produced by the vibrations of the air column in the tube connected with the patient produce an interference of the waves of light as they pass between the mirror and lens. The light used is a monochromatic mercury light with definitely known wave lengths. This interference of light is shown as varying rings and curves in the lens and is photographed on a moving film.

Still more recently Lutembacher has brought out a polygraph run by electricity. The curves are registered by an electric light casting the shadows of the moving pens on a photographic film. The rapidity of the action of light on the film, it is believed, makes this instrument a more accurate recorder of the transmitted vascular waves than the ordinary pen writing. The resulting curves are said to be of great fineness and precision. But the inertia and overfling of the pens still obtain with this instrument.

INSTRUMENTS

Stethoscope.—One cannot pass by the stethoscope as an instrument which has added to the precision of our knowledge in the study of heart disease. As has already been said, it revolutionized the knowledge of the heart and made the practical clinical knowledge of cardiac function an every-day acquisition throughout the profession instead of a knowledge confined to a specialized few.

Laennec's first stethoscope was made from a tube of wood a foot long, cut in two and screwed together in the middle for the convenience of carrying it, the central bore being one fourth of an inch in diameter A perforated plug fitted into the chest end of the instrument, not bell shaped, nor hollowed out conically. There were later many variations of this instrument, especially in the bell-shaped end to fit the chest and in the ear piece with its surface towards the ear being either flat, convex or concave. The substances of which they were made varied from cedar and various other kinds of wood to ebonite, horn, gutta percha or ivory.

Dr. Williams of London seems to be the first who attached two metal tubes to the bell of the stethoscope, the first binaural stethoscope. Landouzy in Paris in 1850 attached several flexible tubes to the bell-shaped chest piece, endeavoring to have several persons listen at the same time, but it did not prove of much practical use. In 1852 G. P. Cammann of New York perfected a practical binaural stethoscope. This stethoscope had the ear pieces fitting snugly into the ears and the metal tubes, running down to the bell piece, ended in two flexible rubber tubes covered by cloth. The two metal tubes were connected by a hinge and held tightly to the ears by a rubber band or by the hand. The improvements of this instrument in use to-day have been to replace the hinge and the rubber band by a steel spring approximating the tubes better to the ear, producing a uniform pressure and allowing freedom to the hands. The internal curve of the bell of the stethoscope is really of great importance, the hollow cone-shaped rubber bell giving very much better sounds than the shallow parabolic curve with a hole in the center.

Bowles' stethoscope consists of a telephone diaphragm screwed onto a metal tambour, this tambour being flat and the hole in its center continuing through a short metal stem over which the rubber tubing slipped and could be attached to the regular binaural stethoscope by a short Y-tube. This has the advantage of being useful with very sick patients who cannot be moved, for the flat, thin tambour can be slipped under the back of the patient as he lies in bed. It also has the advantage of transmitting sounds well through one or more layers of clothing, which the ordinary gutta percha bell of the usual stethoscope does not do.

In appreciating the value of the stethoscope one must realize that in reality the stethoscope should be as individual to the person using it as his shoes, and should fit him, his ears, and his method of thought and interpretation of sounds. It is the evaluation of the sound, as much as the actual sound itself, that has to be considered. There are some sounds that are better heard and their value better appreciated with the ear. This is often true of the breathing, and particularly true of distant bronchial breathing in early pneumonia heard in the center of the lung, particularly in children. There are also soft, diastolic murmurs heard at the tip of the sternum which the ear catches distinctly, but the stethoscope fails to transmit.

Gordon in contrasting the value of the monaural with the binaural stethoscope in the appreciation of cardiac sounds shows that the slight mitral regurgitation murmurs are heard best with the binaural instrument, and the faint aortic murmurs may be missed with the double instrument, but heard clearly with the monaural. He also says that sometimes an aortic regurgitation murmur will be missed by both kinds of stethoscope but heard by the ear. This he says is also true in both the upright and recumbent position of the patient.

Donald M. Cammann considers it an undoubted fact that the habitual use of the stethoscope after a time renders the sense of hearing less acute to sounds heard over the chest, but experience seems to show that it is the habit of the auscultator and his ability to interpret the sounds as he hears them, whether with an instrument or without, that in the end determines the final judgment. It is an acoustic fact that sounds are better heard with two ears than with one, and the binaural stethoscope enables us to use simultaneously the two ears, leaving one or both hands free for percussion. The stethoscope, moreover, can be placed in positions, such as in the super-clavicular and axillary regions, which cannot be reached by the ear. There is no question, however, that the stethoscope enables one to differentiate cardiac murmurs much more accurately than the immediate auscultation with the ear, because one can trace accurately with the stethoscope the transmission of the sounds, and can follow them more accurately to differentiate their finer gradations of sounds.

Phonendoscope.—The phonendoscope, so-called, was a circular metal chamber with a diaphragm placed on the chest which magnified the sounds conducted through the two tubes to the ears, these tubes being entirely of flexible rubber with tips to fit in the auricular openings. This after a short trial did not appeal to the profession as convenient as the binaural stethoscope. It required the use of both hands and magnified the amount of sound rather than differentiating sounds more clearly.

Sphygmograph and Electrocardiograph.—In considering the instruments besides the stethoscope of direct practical value in the every-day diagnosis and treatment of cardiac affections, we come down to two: The sphygmograph or its variations, and the electrocardiograph. To many younger members of the medical profession any explanation of these machines or reasons for their more extended use may seem utterly superfluous. But beyond question since their accuracy and practical value have been established, their use has not correspondingly spread among the profession even in hospitals otherwise well equipped. The expense of the electrocardiograph and the distrust of an electrical instrument not thoroughly understood are sufficient to account for the slowness of the spread of its use. Probably the fact that the electrocardiograph followed so quickly on the development of the polygraph and so far outstripped it in the information given has done much to discourage the use of the polygraph. But now that the cardiac arrhythmias have been differentiated in detail by the electrocardiograph, those which were formerly unsolved by the polygraph can now be recognized by this latter instrument. After a short period of checking up one's clinical observations with these instruments, one learns to recognize many of the arrhythmias without referring to the instrumental proof.

We may sum up our present cardiac knowledge briefly as follows: We know that in childhood and youth the vast majority of cardiac injuries come from rheumatic infection, and we know that 50 per cent of those who suffer from rheumatism acquire cardiac lesions in their first attack. We know that in childhood, before ten years of age, all three tissues, the pericardium, the myocardium, and the endocardium, are often infected at the same time. In youth all three tissues may be simultaneously infected, but either one or two may escape the injury. We know that in rheumatic endocarditis the mitral valve is the most often affected, the aortic much less frequently, the tricuspid still more rarely, the pulmonary valves the most rarely of all. We recognize also the great danger in the mitral infection in that this infection spreading beyond the valve and extending into the muscular tissues around the auriculo-ventricular opening may set up a chronic or subacute process, which, continuing even after the valve lesion has healed, produces the slowly but steadily progressing cicatricial contractions of mitral stenosis. We know also that all infections outside the heart from anywhere in the body are prone to add their injury to the myocardium through toxic absorption, so that after any general disease of the body the heart must recuperate from its own injury. From the early twenties on through middle life the heart is especially in danger from one particular infection, that of syphilis. The aorta, particularly at its junction with the heart and in consequence involving the aortic valves, is the most common seat of this infection. But other valves may be involved, and the myocardium is especially prone to suffer from a new growth of connective tissue peculiar to this infection and to have minute gummata scattered throughout its muscular tissue. All infective processes in muscles when they heal leave cicatricial connective tissue behind, and syphilis is no exception; for luetic aortitis or carditis is as amenable to treatment as any other luetic lesion, and although the lesion has healed the scars are left in the damaged myocardium.

We know that when there are lesions in the valves from whatever cause, there will be an increased mechanical strain thrown on the muscles surrounding the chambers using these valves. The myocardium follows the laws of other muscles and increased work brings increased volume of muscle fiber, and all muscle fibers must stretch and lengthen to do increase of work. Hence, hypertrophy and dilatation are at times an expression of physiologic function more than of pathologic injury. Unfortunately all hypertrophy may not be of muscle increase, for the inflammatory lesions cause at times great increase of connective tissue and the increase of size may not mean increase of power, but indicate the reverse. After middle life is passed even in those who have escaped the injuries of infections, atheromatous changes may appear in the aorta and blood vessels, and the aortic valves or even the mitral suffer from these degenerative changes. The aorta and, leading from it, the coronary arteries show these senile degenerative changes. Syphilis, it is true, may have caused an early arterial degeneration, or acute or chronic septic infections may have caused the aortitis. At whatever time of life, from whatever cause, infection or degeneration, many a heart receives its final " coup de grace " from the sudden blocking of some part of a coronary artery. We know that the right and left coronary arteries not only anastomose with each other very freely, but branches of each artery also freely anastomose. We know also as the decades of life accumulate, the right ventricle loses its finer vascular supply while the left ventricle gains an increase. Post-mortem examinations show that after the blocking of even a main coronary artery life may go on for years, but usually the blocking of a main branch is sufficient in a few hours or days to cause death. We know that in some patients the blocking of coronary vessels brings with it terrific pain, and yet again others seem to suffer the same or analogous lesions without pain. We have no instruments to measure the amount of pain nor any clue as yet as to why it arises in some lesions of the heart, or why it does not occur in other lesions. We know also that the heart is under nervous control and intensely sensitive to emotional influences. The cause of its beat we do not know, but we know that the stimulus to set it in motion arises near the junction of the superior vena cava and right auricle, and spreads by a special conducting system separated from the main mass of its powerful contracting muscles, and joins auricles to ventricles by the single auriculo-ventricular bundle of muscle and nerves. This bundle divides in the interventricular septum into a right and left branch going to the corresponding ventricle, ramifying as the Purkinje fibers over each ventricle, thus connecting with the muscular contracting mass, and supplying the stimulus to contract. Disturbances of normal function are expressed in diminution, cessation, or increased irritability of cardiac function. These disturbances of function may be evident in either auricles or ventricles or in their connecting bundle, and when producing irregularity of cardiac action, or incoordination between auricles and ventricles are recognized clinically as the cardiac arrhythmias. These irregularities we can measure with instrumental precision and differentiate their origin whether they occur in the sinus or auricle or bundle of His or in either ventricle. This the polygraph, or especially the electrocardiograph, will do. These two instruments give similar information although measuring entirely different cardiac phenomena. The polygraph measures the volume curves in venous and arterial pulsations. Each curve taken alone fails to supply the desired information, but when the details of the venous are compared with the details of the arterial curve in strict regard to their simultaneous occurrence in the known cardiac cycle of events, information is obtained regarding (1) the frequency and infrequency of the heart's action, (2) the regularity or irregularity of its rhythm and the force of its beat, (3) the origin of the irregularity, whether it arises in the auricle, bundle or ventricle, (4) the time required for the impulse to travel from auricle to ventricle through the auriculo-ventricular bundle, (5) the relation to the whole cardiac cycle of the auricular and ventricular systoles and their diastole.

There is nothing characteristic in any detail of the venous polygraph curve to show which curve is due to auricular or which due to ventricular contractions. There is no possible way to distinguish whether the auricular impulse starts from the sinus or from somewhere else in the auricle, nor is it possible to tell from which ventricle the extra-systole arose.

The electrocardiograph, however, is based not on the volume waves in the blood-vessels or tissue vibrations, but on the fact that a difference of electric potential arises in contracting muscles, and the part contracting is negative to the uncontracted part. In the heart such a condition arises when the stimulus starts from the sinus auricular node just previous to contraction and spreading down the neuromuscular system and Purkinje fibers causes the cardiac contraction. The longer the time for the excitation wave to pass between the electrodes, the greater the difference of potential and the greater the extent of movement of the string. The extent of the movement is not therefore in proportion to the strength of contraction, but to difference of potential. The resulting electrocardiograms are accurate pictures of the variation of electric potential as the stimulus passes along its normal or usual, or abnormal or unusual channels. Any variation from normal of the origin of the stimulus or a lengthening of the time of its passage or a failure to pass along its customary route are shown by characteristic curves.

The electrocardiographic curves, however, are but the expression of the excitation wave as it passes through the heart. They are not the expressions of the contraction of the heart, and there is no instrument that measures the amount of contracting power left in a damaged myocardium nor, as a matter of fact, in the normal muscle.

Physiology of the Cardiac Cycle.—Before starting the study of any cardiac irregularities or the interpretation of any polygraphic or electrocardiographic curves, there are certain general physiologic facts to be remembered, and though well known should not be left unsaid. The first of these is that the two auricles beat as one and the two ventricles as one; that the heart beats normally in regular rhythm and the rhythm may change normally, be fast or slow; that normally the most irritable point of the heart is the sinus at the root of the superior vena cava, and the stimulus passes thence through the auricle to the auriculo-ventricular node, and from there down the bundle of His to its right and left branches, spreading over the right ventricle in a clockwise manner, and over the left ventricle in an anti-clockwise manner. This impulse spreads, moreover, over the inner surface of the ventricles, conducted in both instances by the Purkinje fibers. If either bundle is defective the excitation passes down the uninjured bundle and apparently around on the surface of the heart to the other ventricle. Normally the auricles contract first, then with a momentary pause they are followed by the ventricles. If, however, for any reason some other point in the auricle becomes more irritable than the sinus, it may start a contraction before the stimulus in the sinus begins, and if repeated sufficiently rapidly may control the rhythm of the heart. From these abnormally irritable areas the ectopic beats occur and the paroxysmal tachycardias.

The same is true of the auriculo-ventricular node or the bundle near the node between the auricle and ventricle. Single foci of increased irritability may cause contraction before the regular beat of the auricle through the sinus takes place. This is also true of either the right or left bundle and they may develop foci of increased irritability and bring about ectopic right or left ventricular beats.

Cardiographic Curves.—In electrocardiographic curves these different occurrences are registered by characteristic differences of the curves which will be mentioned later. In considering polygraphic curves there are certain other factors in the heart that should be remembered. One particular feature in the heart which exerts more influence on the jugular curve than is usually appreciated is the movability of the fibrous ring at the junction of the auricles and ventricles and the movability of the floor of the auricles or the top of the ventricles. The heart is held at a fixed point by the great vessels above. Another fixed point is at the apex because of the peculiar whorl-like arrangement of the ventricular muscles. When the auricle contracts it pulls the fibrous ring and its floor upward, thus diminishing the size of its cavity and enlarging the cavity of the ventricle below it. It acts as if it were pulling up the ventricle over the mass of blood which is being driven into it. As the auricle relaxes blood from the veins flows into it. When the ventricle contracts it pulls the fibrous ring down, diminishing the size of its cavity, and forcing the blood out through the aorta and pulmonary artery, at the same time increasing the size of the cavity of the auricle and causing an increased supply of blood to come into the auricle from the veins and increased rapidity of the flow from this source. As the ventricle relaxes in diastole, just before the contraction of the auricle as the tricuspid and mitral valves open, the cavities of the two chambers on either side of the heart are one. This movement of the fibrous ring between auricle and ventricle causes sudden variations in the pressure of the veins above the heart, and the increased flow and check of this flow by the movement of this partition between the auricle and ventricle has a marked influence on the jugular curve in the tracings, both in forming the depressions x and y and in the formation of the V waves.

A sphygmograph in reality is an instrument which gives a graphic description of the pulse, and a polygraph is a sphygmograph giving several curves at the same time. The only instruments to-day of practical value are the polygraphs, which register the curves from the jugular vein or from the radial or brachial artery simultaneously, or with the same instrument one can at the same time register the apex beat. These curves require an accurate time marker, usually of one fifth of a second, to enable one to judge accurately of the normal sequence of events in the cardiac cycle. The time is past when the cumbersome revolving drum with its blackened paper is of practical value. The time is also past when the smoked paper in the beautiful little Jaquet instrument need be used. Mackenzie's modification of using white paper and pens which write in ink have solved the bothersome trouble of smoking a paper, of carrying it uninjured and smooth to the bedside, and after the record is taken of soaking it in shellac to keep it from being rubbed off and destroyed. The time has passed also when instruments which use the small metal button to press upon the radial pulse need be used. They are tantalizing wasters of time as compared with the rubber cuff to record the brachial pulse or the most recent modification of the Mackenzie-Lewis polygraph, using a wrist cuff with a glycerine transmitter for obtaining the curves of the radial artery.

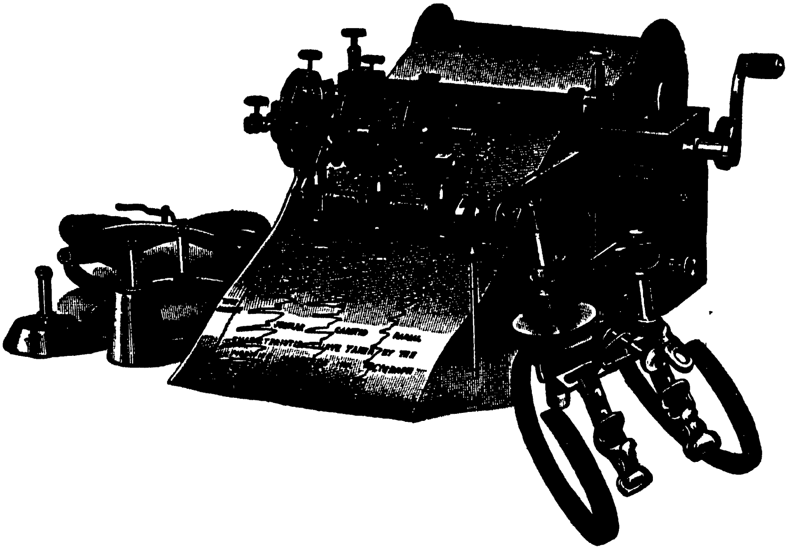


FIG. A. MACKENZIE INK POLYGRAPH. (From Lamson, The Heart Rhythms, Courtesy Williams and Wilkins Company.)

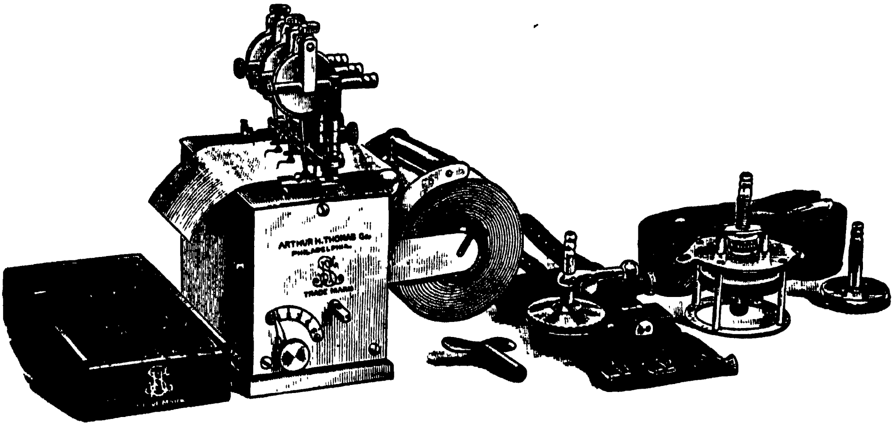


FIG. B. JAQUET PORTABLE POLYGRAPH. (From Lamson, The Heart Rhythms, Courtesy Williams and Wilkins Company.)

There are several excellent instruments in the market; Dressler's American modification of Mackenzie's polygraph is such an instrument, having also a blood-pressure attachment to record simultaneously with the vascular curves the variation or value of the systolic pressure. Its

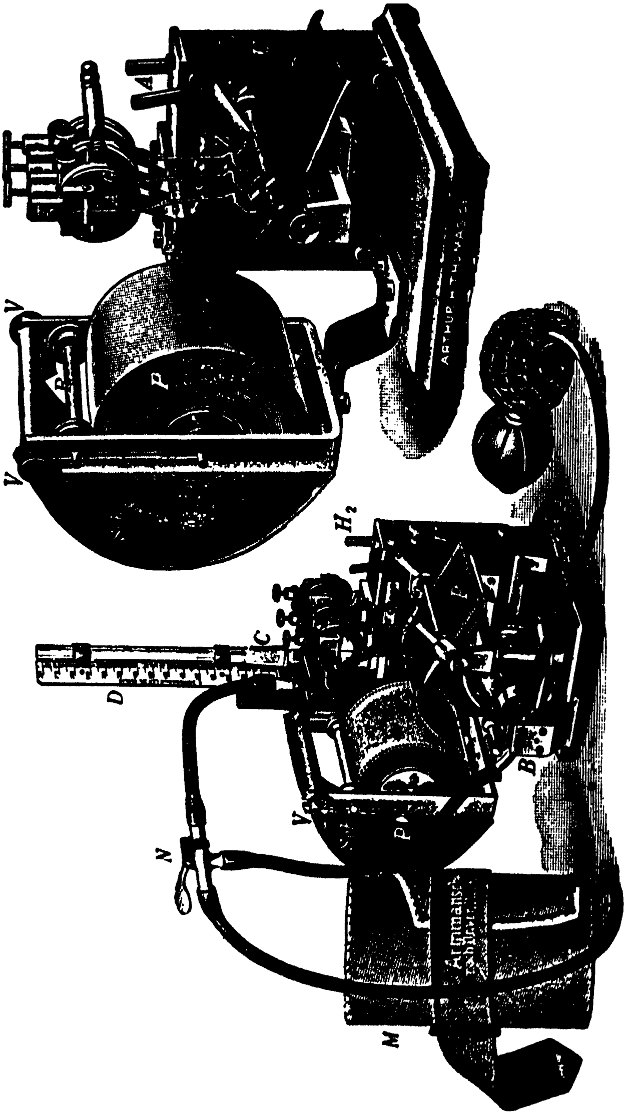


FIG. C. THE ZIMMERMAN POLYGRAPH. (From Lamson, The Heart Rhythms, Courtesy Williams and Wilkins Company.)

pens are run horizontally on the paper. Mackenzie-Lewis's new polygraph is also excellent and compact. When the box is open it is ready for use without loss of time. Its pens also write horizontally. Lamson recommends the Zimmermann polygraph. Its pens write vertically so that gravity aids in giving smoothness to its records, and he ascribes to this instrument the ability to give perfect curves. It also has a blood-pressure attachment.

Of the two instruments mentioned as eliminating the inertia of the movement of the pens and the overfling of their record, that is Franck's optical capsule or Crehore's micrograph, the instrument of Franck mounted on a table to move around the hospital is of the two the more practical. The micrograph consumes too much time and does not give increase of knowledge commensurate with the expenditure of time for its technic. It seems to give more detail of many vibrations, but as already stated, an increased detail is not, beyond a certain extent, the

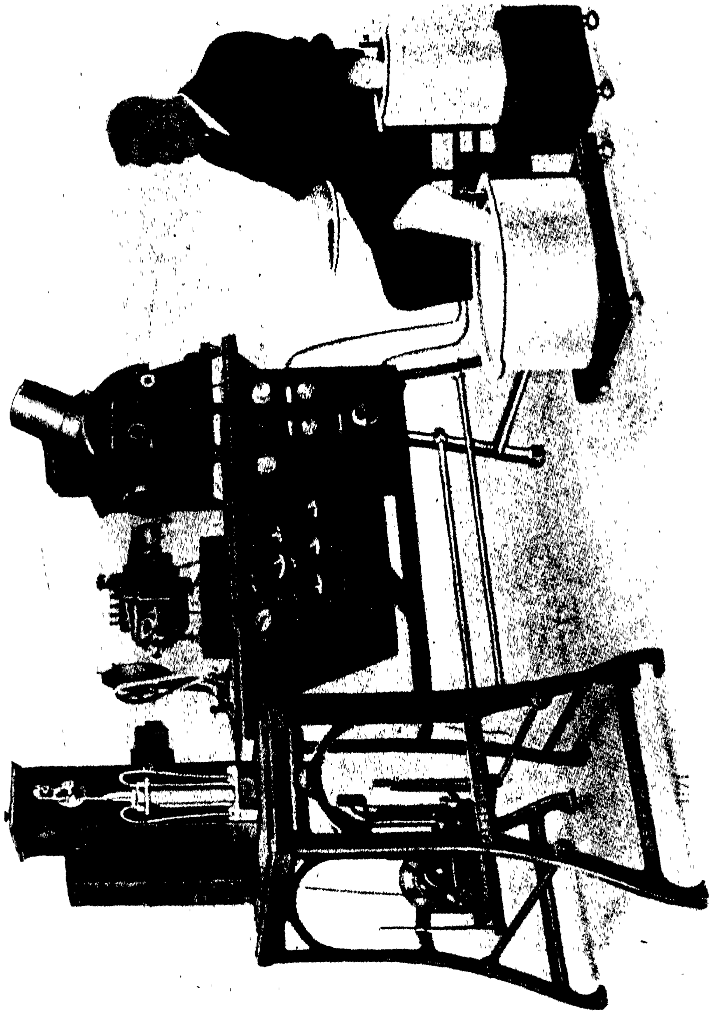


Fig. D. Complete Electrocardiograph, Showing the Manner in Which the Electrodes are Attached to the Patient. (From Lamson, The Heart Rhythms, Courtesy Williams and Wilkins Company.)

essential knowledge desired in polygraphic records, and fortunately the simpler instruments give us adequate knowledge for a differentiation of the majority of the cardiac arrhythmias.

METHODS OF TAKING TRACINGS.—The accompanying illustrations of the various instruments are sufficient for their description. They all show the rubber cuff slipping over the hand to obtain either the radial curve at the wrist, or the brachial curve on the upper arm. They further show the tube going from this attachment to the tambour with its rubber membrane stretched across its face, to which is attached the pen that the vibrations transmitted through the tube to the tambour may be recorded as a curve by the pen writing on the moving paper. For the jugular vein there is a glass funnel used instead of the cuff, and this should be inserted just above the sterno-clavicular joint where the jugular bulb shows in the neck. Care must be taken that the sterno-mastoid is sufficiently relaxed to obtain a good curve by bending the head slightly forward, and care also must be taken that the real jugular tracing is obtained and not by too energetic pressure so that the glass funnel rests upon the carotid artery and records an arterial curve instead of the venous. An apex curve may also be obtained in a similar manner to the venous curve by having a band encircle the chest to hold the receiver against the chest over the apex area or it may be held by the hand, an assistant starting the lever of the machine. It is always necessary to have an ordinate to these curves, that is, the pen should be made to move simultaneously and at right angles to the curves, across the paper on which the curves are to be recorded lengthwise. This gives a point in each curve from which to calculate synchronous occurrences, and this is absolutely essential for the comparison of the jugular with the radial or brachial curve.

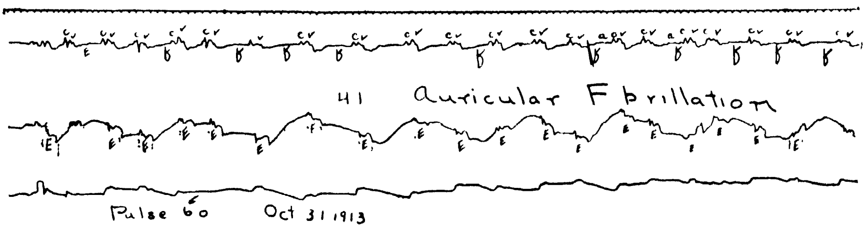


FIG. E. POLYGRAPHIC TRACING SHOWING AURICULAR FIBRILLATION.

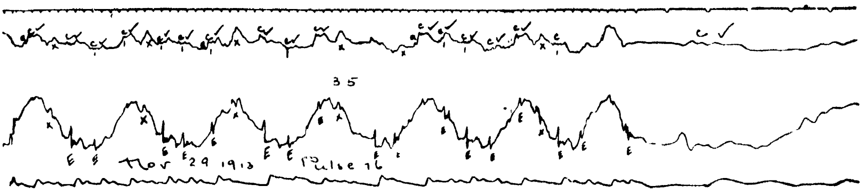


FIG. F. AURICULAR FIBRILLATION WITH VENTRICULAR EXTRASYSTOLES.

Reading of Tracings.—A single tracing of radial or jugular or apex gives little information of real value beyond the regularity of the rhythm of the heart. As has been already said, it is only by comparison of the venous curve with that of the apex or the radial that full information may be obtained. The venous curve, however essential as a comparison, has nothing characteristic, whether it be produced by auricle or ventricle. The radial curve has two characteristic points: first, the beginning of the rise of the pulse, which shows the arrival at the wrist of the systolic wave, and second the dicrotic notch, which occurs at the time when the semi-lunar valves close. The space between these two points on the curve, therefore, is the duration of the cardiac systole.

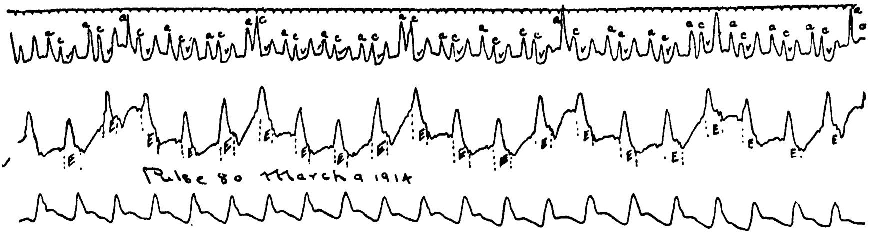


Fig. G. Slight Pulsus Alternans in Acute Rheumatism.

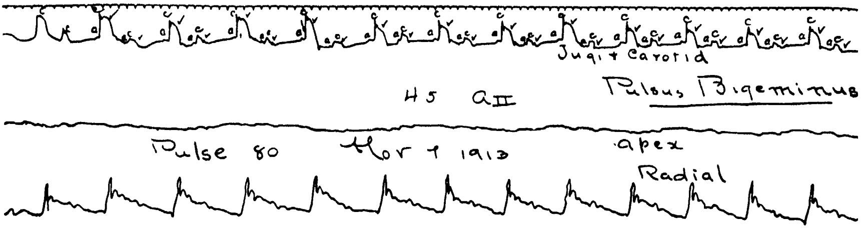


Fig. H. Pulsus Bigeminus.

As Lamson points out, these two points are the only known points in the curves, and from these two must be calculated the relationship of the other waves.

In the venous curve there are three waves, which are always to be considered, and occasionally in slow-beating hearts a fourth one. These are known as the A, C, and V waves, and occasionally the H wave of Gibson and Hirschfelder. The A wave represents the contraction of the auricle and is caused by the reflux of the blood in the veins as the contracting auricle prevents the blood flow onward, and sends a wave backward. It occurs one fifth of a second before the C wave. Mackenzie claimed that the C wave was due to the pulsation of the carotid, but physiologists disagree with this, and it has been shown by Straub that it occurs in the intra-auricular curves, and it also shows in the jugular when the carotid on that side of the neck has been removed. Whatever its origin it occurs at the time of the contraction of the ventricles, and is a wave signifying the ventricular systole.

The V wave occurs with its summit two fifths of a second after the point at the beginning of the C wave. It is really a wave formed by the sudden emptying of the veins rather than a direct pulsation.

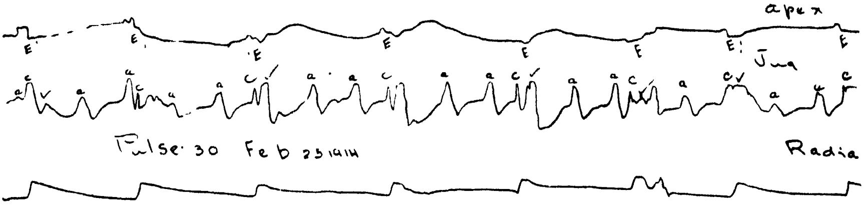


FIG. I. HEART BLOCK.

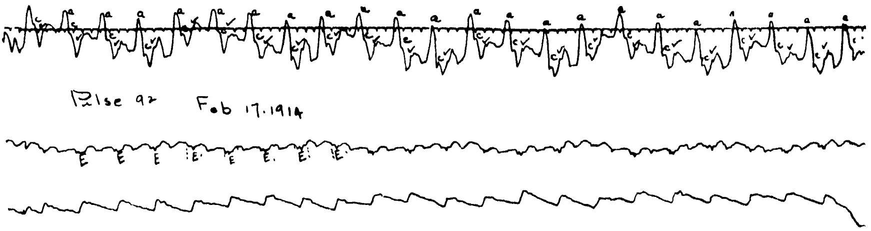


FIG. J. TRICUSPID REGURGITATION.

It occurs at the time when the auriculo-ventricular valves open and the blood drops out of the auricle into the ventricle, and the veins in the neck emptying quickly produce the sudden fall of pressure, giving it the appearance of a wave, when it is really a curve formed by a cessation of pressure, not a positive reflux wave. The V wave is not always a single wave, but is frequently double. At the same time as the V wave falls, the dicrotic notch occurs in the radial tracing, and this dicrotic notch corresponds exactly with the point just after the apex of the V wave.

The H wave of Gibson and Hirschfelder is a small wave, usually single, occurring in the venous tracing between the V and the succeeding A waves. It usually occurs about 0.5 to 0.6 second after the A wave. It usually occurs in slowly beating hearts, and is believed to be due to the floating up of the tricuspid valve and its closure by inrushing blood, thus giving a sudden closure of the auriculo-ventricular opening with a reflux wave in the veins. It may fall midway between two auricular waves and be mistaken for partial heart block with failure of every other auricular wave to cause ventricular contracture.

Considering these waves A, C and V as wave crests of a general curve, there are the depressions or troughs between these waves. The depression between the A and C waves is usually small and frequently C is only a slight rise at the end of the A wave, or on the falling curve of A. It may, however, be the dominating wave. At times there is a

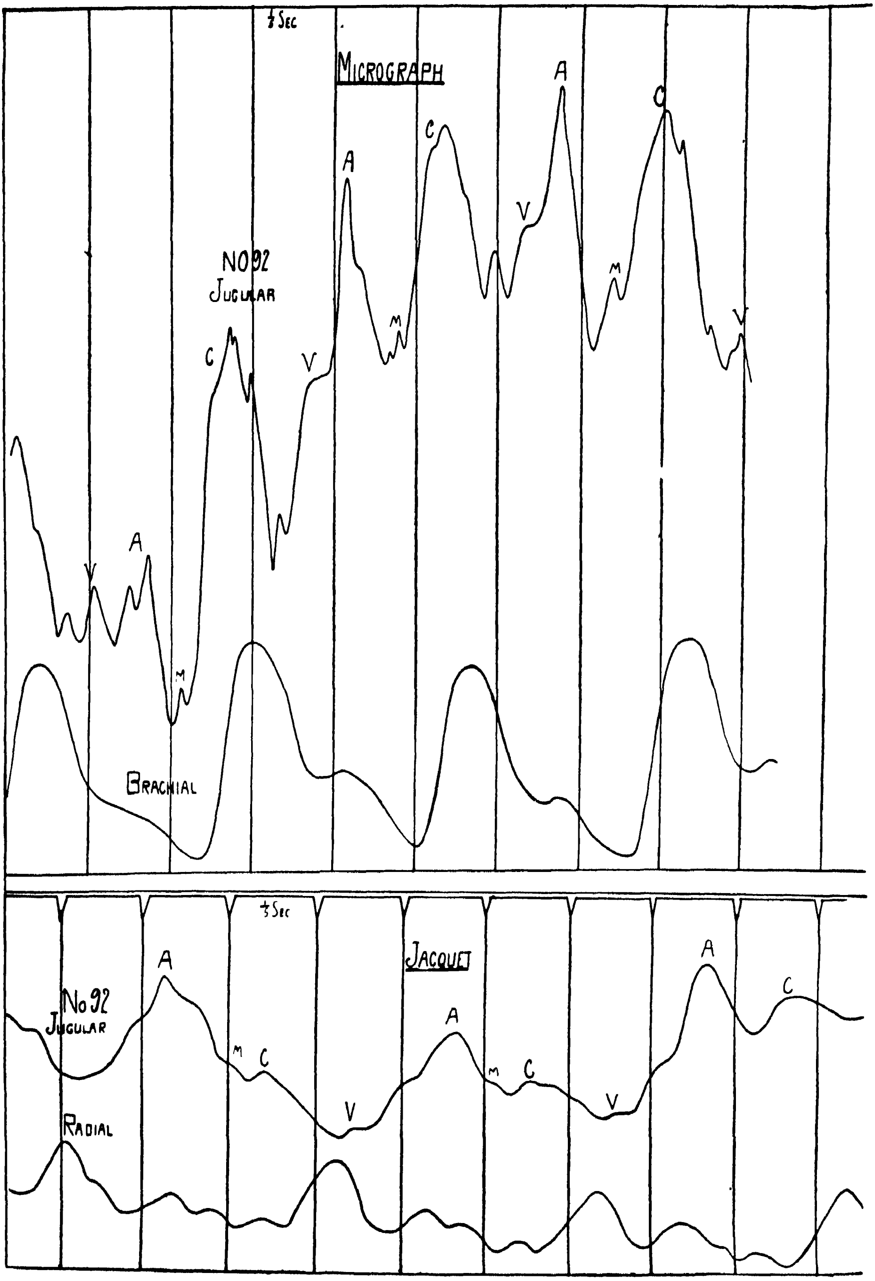

⅕ Sec
Micrograph
A
C
A
C
V
A
No 92
Jugular
C
V
M
M
V
A
V
M
Brachial
⅕ Sec
Jacquet
A
A
No 92
Jugular
M
C
A
C
M
C
V
V
Radial

Fig. K.

slight wave between the A and C waves, this is referred to by Flint as an H wave, but was observed by Crehore with the micrograph curves, and named the M wave by him, as he believed it due to the closure of the auriculo-ventricular valves at the moment between the auricular and ventricular systoles.

Between the C and V waves in venous tracings there is the depression X formed by the reduction of pressure in the jugular vein as the blood flows into the empty auricle, and this chamber evidently fills quickly as the rise forming the V waves occurs and is formed by the blood held in the auricle and veins during the systole of the ventricle, and V waves are formed at the cessation of ventricular systole by the emptying of the blood into the relaxed ventricle, thus giving the depression Y and in slow beating hearts as the tricuspid valve is floated closed by the blood the wave H is formed during the diastole of the heart.

Measuring of Tracings.—In measuring out a normal polygraph curve the method of Lamson is the simplest. Just before beginning a tracing, or at the end of one, or at some definite point during a tracing before starting the clock-work, or after it has ceased, the two pens which write the different tracings must be permitted to move simultaneously forming two lines at right angles to the curves. As emphasized above, this gives two ordinates from which to measure synchronous occurrences in the two curves. To measure a curve, therefore, one takes a pair of compasses and measures from the ordinate on the radial curve to the point at the beginning of the rise of a single radial pulse tracing. Then measuring back a distance equivalent to one-tenth of a second on the paper, one has the point which corresponds to the beginning of the C wave in the venous curve because it takes the blood one tenth of a second practically to go from the ventricle to the wrist. The left-hand point of the compass is then placed on the ordinate of the venous curve, and the right-hand point of the compass should correspond to the beginning of the C curve belonging to that radial pulse.

In the venous pulse curves the wave occurring just previous to the C wave, beginning one-fifth of a second previous to it, is the A wave or auricular contracting wave. In the same manner measuring from the radial ordinate to the dicrotic notch and transferring that distance to the venous curve, the right hand point of the compass should fall on the downward side of the crest of the V wave. The crest of the V wave in normal phlebograms is two-fifths of a second beyond the beginning of the corresponding C wave.

Mackenzie's standards for interpreting the venous pulse are based on a comparison of simultaneous events in the jugular pulse, the apex beat, the carotid and the radial pulse. These points are indicated by numbered perpendicular lines, and always have the same significance in all his tracings.

1. The beginning of auricular systole. The beginning of the A wave in jugular tracings.

2. The beginning of the ventricular systole. The beginning of the rise in apex beat tracings.

3. The appearance of the pulse in the carotid. The beginning of the C wave in the jugular and the beginning of the rise in carotid pulse curve.

4. The appearance of the pulse in the radial. The beginning of the rise in the radial pulse curve.

5. The closing of the semilunar valves. The notch between V^1 and v^2 in the jugular tracing and the dicrotic notch in the carotid pulse curve.

6. The opening of the tricuspid valves. A point on the falling side of v^2 in the jugular tracing and the dicrotic notch in the radial pulse curve.

The space between 2 and 3 is called D, the presphygmic period of the ventricular systole.

The space between 3 and 5 is called E, the sphygmic or pulse period, the period of ventricular output.

The space between 5 and 6 is called F, the post-sphygmic period.

The space between 6 and 2 is called G, the period of ventricular diastole.

The space between 1 and 3 is called the A-C interval and is taken as the measure of the time it takes the stimulus to pass from auricle to ventricle.

Mackenzie recommends taking, with each jugular and radial tracing, a short tracing of the carotid pulse to obtain the distance on the radial between points 3 and 4; i.e., instead of measuring back $\frac{1}{10}$ second from the point of the beginning of the radial rise to measure the exact distance between the beginning of the carotid and radial pulses.

Significance of Various Curves.—All jugular curves showing the A wave are called auricular types of venous curves. When the A wave is absent the jugular curve takes on the ventricular type of venous tracings. There are two varieties of ventricular type: one, showing a large single V wave synchronous with ventricular systole, and one great depression, y, synchronous with ventricular diastole. When the rhythm is regular with the long diastolic period there is a rise in the tracing due to the vein filling. The second variety shows a mid-systolic fall so that there are C and V waves. These ventricular types of venous pulse occur when the auricle does not contract or its contraction is not vigorous enough to influence the pressure in the veins.

Mackenzie gives as the three conditions which produce ventricular forms of venous pulse: (1) auricular fibrillation, the most common cause; (2) great distention of the right auricle from engorgement of the right heart; in these cases the rhythm is regular and the A wave reappears when the engorgement subsides; (3) certain forms of tachycardia starting from ectopic foci produce such engorgement of the heart that each ventricular systole sends large waves of blood through the auricle to the vein.

It is well to remember that changes in rate cause changes in the venous curves. The shortening of the cycle takes place mainly in the diastolic portion of the curves. The first change to occur is the elimination of the space between the V and A waves and the A wave follows closely after the V. If the rate increases further the V and A waves may become blended and the depression y disappears.

In the interpretation of unknown polygraphic curves unless one is very familiar with all known curves and can rule out at a glance by exclusion many curves. it is necessary to follow a routine procedure to make a diagnosis of any given polygraphic curve. In the first place, it is necessary to measure the distance marked off by the time marker to see whether or not the paper has been running smoothly and regularly so that the time marker indications are equidistant. If these are at all irregular in this, it may throw out of accuracy any measurements made at supposedly synchronous distances. It is also, to begin with, necessary to note the radial tracing to see if it is regular both in its rhythm and the force of its contraction.

Cardiac Arrhythmias.—Flint gives an excellent skeleton to be followed, in which the classification of all various forms of cardiac irregularity and abnormal rhythm are mentioned, and he recommends that in solving a difficult tracing this list should be worked through systematically.

The most logical method of considering cardiac arrhythmias is to begin at the sino-auricular node, follow the impulse through the auricle to the auricular ventricular node, consider then the blocking of the impulse on its way to the ventricle, then follow down the bundle to the ventricle, and deal with all possibilities in this order.

One realizes in this way that the number of possibilities is distinctly limited, and can be theoretically conceived, and these theoretical considerations found occurring in practice.

NORMAL RHYTHMS.—Beginning with the sino-auricular node, we realize that it possesses four rhythms: the normal rhythm; the increased rhythm or the physiologic tachycardia due to exercise, or from whatever cause; the bradycardia, normal in some people; and sinus arrhythmia which is the regular or irregular variation of the rhythm usually during respiration, and ceasing in this case if respiration is held.

The polygraph shows a regular sequence of events, a normal time between auricle and ventricle and a variation simply in the rhythm, fast or slow, as the pulse varies in frequency.

AURICULAR IRREGULARITIES.—The sinus node normally controls the rhythm of the heart, but sometimes its rhythm is interrupted by some sudden irritation showing as a premature explosion in the sinus or in some of the conducting tissue, or even when the tissue of the auricle itself is more irritable than the sinus, and a premature explosion occurs causing a contraction of the auricle. This sends an impulse down the bundle to the ventricle, and may cause a ventricular contraction out of rhythm, if it arises at the ventricular muscle when it has gathered suf-

1. **Normal rhythms:** **Normal tachycardia.**
   - **Normal rhythm.**
   - **Normal bradycardia.**
   - **Sinus arrhythmia.**

2. Auricular interpolated beats or escaped ectopic beats.
   - Auricular premature beats with normal relation to ventricular contraction.
   - Auricular premature beats blocked by failure of ventricle to contract.
   - Auricular multiple ectopic beats.
   - Auricular paroxysmal tachycardia.
   - Auricular flutter.
   - Auricular impure flutter.
   - Auricular fibrillations.

3. Sino-auricular block.
   - Delayed auricular ventricular conduction.
   - Partial or varying AV block.
   - Complete AV block with disassociated auricular and ventricular rhythms.
   - Interauricular block.

4. Nodal premature beats.
   - Nodal rhythm.
   - Nodal paroxysmal tachycardia.

5. Ventricular ectopic beat.
      1. right ventricle.
      2. left ventricle.
   - Alternating right and left ectopic beats from same foci.
   - Alternating right and left ectopic beats from shifting foci.
   - Coupling with ectopic beats, pulsus bigeminus.
   - Tripling with ectopic beats, pulsus trigeminus.
   - Ventricular escapes or interpolated beats.
   - Ventricular tachcardia from
      1. right ventricle.
      2. left ventricle.
   - Bundle block
      1. right.
      2. left.
   - Pulsus alternans.
   - Ventricular fibrillation.

Flint's Classification of cardiac irregularity, normal and abnormal rhythm.

ficient energy to contract again, i.e., when it is not refractory. These contractions are always premature to the normal time, and are therefore sometimes called premature beats; they have usually been called extra systoles, because they seemed clinically like extra beats thrown in between the normal frequency of rhythm. There is a tendency at present to agree to call these beats ectopic beats. The polygraph does not show whether these beats arise in the sinus or the adjacent tissue, as will be seen in the electrocardiograph. These beats are single or multiple in occurrence, in both auricle and ventricle, and at times seem to show a rhythm of their own.

Premature auricular contraction may be followed by pauses of three lengths, a pause equal to the interval between rhythmic contractions, or a pause truly compensatory or a pause of intermediate length.

In the first instance when the ectopic auricular contraction is followed by an interval which is exactly equal to the interrupted rhythm, it means that the sinus has gone on again with its rhythm, and only one beat is out of time. It is practically an interpolated beat, or auricular escape. In these polygraphic curves each auricular contraction is followed by its corresponding ventricular contraction as shown in the radial curve.

In the second instance the pause following the ectopic beat is longer than the regular spaces between the rhythmic contractions, but only just sufficiently so as to make the distance between the beat following the premature contraction and the last rhythmic contraction before the premature beat equal to the regular interval between any two other rhythmic contractions. In other words, the beat following the premature beat occurs at the time that compensates for the previous irregularity. This is not usual in auricular ectopic beats, but is the usual occurrence in the ventricular ectopic beats. The usual spacing between contractions following an auricular ectopic beat is of intermediate length, so that there are usually two beats out of rhythm.

The third instance here is so usual in auricular ectopic beats that it is given as the characteristic differentiation between the auricular and ventricular ectopic beats.

In paroxysmal tachycardia we have ectopic beats following each other from some focus with such rapidity that the dominating rhythm is taken away from the pace-maker of the heart, and controls the cardiac rhythm over the sinus. These come from some point in the auricle outside of the sinus but the polygraph does not show this. As far as the polygraphic curves are concerned, it is a series of rapid, regular auricular contractions followed by regular ventricular contractions, the same as if it were an ordinary tachycardia of normal sinus origin.

There is another condition occurring in the auricle arising in some point outside of the sinus in which the rapidity of the auricular contraction is usually about three hundred. It is known as auricular flutter; its relation to the ectopic beats and the paroxysmal tachycardia is not understood. The rapidity of its rhythm is such that all impulses do not go through the auricular ventricular bundle and cause a ventricular contraction, they are blocked by the AV node whose length of refractory period is high. But it is not entirely because this rhythm of flutter is running so rapidly; for there have been cases of flutter in which the rhythm was only 130 per minute, and the ventricle can easily contract at that rate.

From the work of Lewis and his co-workers, it is evident that a single excitation wave may pass more than once through the same tissue, and that two or more beats may result from a single impulse. They have further shown that an impulse started at one point may follow round in a circle and arrive at the point of origin, and find its further continuance blocked by the refractory condition of the muscle, or arrive just as the muscle is losing its refractory condition and follow around again in the same path. This refractory condition of the contracting processes, and the varying stages of the refractory condition of the muscle causes in the case of flutter an even circling of the contraction in the same path, going only at certain regular intervals down the bundle to the ventricle as the slowness with which the refractory state of the AV node wears off and permits transmission.

In the case of impure flutter with contractions at unequal intervals and with rhythmic irregularity, being blocked by greater masses of refractory muscle, the impulse takes a more sinuous path through the muscles of the auricle. If the rate of contraction becomes greater than in flutter, and the masses of muscle in refractory condition become larger, the more rapid contractions are so blocked that there is a sinuousity of course taken by the contracting impulse through the muscles of the auricle. This produces still greater irregularity of the spasmodic contractions which send impulses irregularly, and without any definite rhythm to the ventricle and is known as the condition of auricular fibrillation.

The polygraph shows in flutter a definite rhythmic number of evenly running contractions, with two, three, or four contractions of the auricle to one contraction of the ventricle, and the A wave will show in corresponding frequency in the venous pulse with the radial pulse showing a smaller number of ventricle contractions.

In impure flutter the A waves are equally prominent with no regularity, and in auricular fibrillation there is absolute irregularity of the ventricular beat as shown in the radial, and the A wave is usually entirely absent from the venous pulse.

Beside the block occurring in auricular fibrillation and flutter from a refractory condition of the muscles, there also occurs either from vagal inhibition, or from other causes, a block at the sinus auricular node which would show as infrequent beats, but when the beats once come, they go through regularly to the ventricle without further interruption. The polygraphic curves appear as if there were a long gap between beats. There can also be a block at the auricular ventricular node, hindering or preventing the impulse going through to the ventricle, the degree of this block also varies, and a time longer than two-tenths of a second occurs between the auricular wave A and the systolic or C wave in the vein. To measure this delayed conduction, the distance between the beginning of the A wave and the beginning of the C wave is taken, which should be not more than one-fifth of a second. Where the impulse is delayed, a greater distance between these points is shown.

Flint quotes Dr. Wardwell Griffith as giving a more accurate method of measuring this AC interval. It is claimed for this method that it has the great advantage of being independent of the point at which the auricle begins to contract, and also the origin of the C wave. Griffith calls it "the summit of the auricular wave to the beginning of the radial rise measurement." Measure with a pair of compasses from the ordinate at the beginning of the jugular tracing to the summit of the A wave, and transfer this measurement to the radial tracing then the distance from this point to the point 4, that is to the beginning of the radial rise, is the meaurement of the true AC interval.

Heart Block.—Often, as in acute rheumatism or in beginning digitalis poisoning, the delayed conduction is one of the earliest signs of beginning of partial or complete block, and the AC interval is an important measurement. At times the impulse is delayed more and more for several successive beats, and then with the increasing prolongation of the AC interval, and finally an impulse is blocked, and the A wave of the venous curve has no C wave corresponding to the wave in the radial pulse. Delayed conduction is shown by prolongation of the AC interval, and partial block is shown by some impulses from the auricle being blocked and others going through the auricular ventricular node to cause a ventricular contraction. Where there is a complete block and no auricular impulses pass to ventricle, the ventricle takes on a rhythm of its own. The ventricular tissue, however, being less irritable than that of the auricle, the ventricular rhythm is always slower than that of the auricular. There is then an auricular rhythm running with perfect regularity, but absolutely independent of the ventricular rhythm which also runs with perfect regularity, and the A waves in the venous curve will show no relation to the ventricular contractions in the radial pulse. In these cases of complete block it is also possible to obtain irregularity of rhythm, and it also is possible to have auricular ectopic beats as well as ventricular ectopic beats. It is also possible for an auricle to be in auricular fibrillation, its irregularities blocked at the node, and the ventricle pulsate with its regular rhythm, or even again the ventricle be interrupted in its regularity by ectopic beats from either ventricle.

At times the ectopic beats may arise in the node itself; this would cause a simultaneous contraction of the auricle and ventricle, and would be shown in the syhygmographic tracing as a very large combined A and C wave. The former nodal rhythm of Mackenzie with paralysis of the auricle proved to be auricular fibrillation.

VENTRICULAR ECTOPIC BEATS.—At times the ventricle will contract out of time, the contraction not being caused by an impulse from the auricular beat. These ventricular extra systoles or ectopic beats are of two kinds; one is where they occur prematurely, and the beat following it waits for its auricular impulses and contracts with a typical compensation. In this instance there are no extra beats, there are simply two beats out of time. In the other instance there is an interrupted beat, as in hearts beating slowly there may be an ectopic beat occur without auricular stimulation, and then followed by the regular rhythm at the regular time. This gives a real extra beat, and is an interpolated beat or ventricular escape. The polygraph shows an extra impulse in the radial curve from the ventricle, but without a corresponding A wave.

There also occurs at times from ectopic foci in the ventricle, paroxysmal tachycardia. This cannot be differentiated except by the electrocardiograph. Ventricular fibrillation, which is not consistent with life, has also been reported from electrocardiographic curves.

PULSUS ALTERNANS.—There is one condition which the sphygmograph shows better than the electrocardiograph, and that is the condition of pulsus alternans, in which there is an alternation of strength between succeeding beats, showing in the radial curve an alternating stronger and weaker pulse wave indicated by varying heights of the radial impulses. This may occur in every other beat or show as one strong beat followed by two or more weaker beats.

Crehore Micrographic Curves.—Just before the electrocardiograph came in general use, Crehore and Meara described a micrograph, which used the interference of the wave lengths of the monochromatic light as a means of measuring cardiac impulses. The following curves were obtained with this instrument. They give the same curves as the polygraph and were compared both with the Jacquet polygraph and later with the electrocardiograph. The photographic film as it is obtained is shown in figure K.

The distance between markings is measured and marked off on plotting paper; the shortness of the film gives but few beats which is a great disadvantage, and the time required to plot the curves is so considerable as to render it an impracticable instrument for clinical use in the wards of a hospital.

The curves given, however, show not only what is indicated in an ordinary polygraph, but are interesting in that they also show vibrations that the ordinary polygraph does not transmit or which are not taken account of in the ordinary interpretation of the curves.

Jaquet Curves.—The following Jaquet curves are given as they were made out according to scale for comparison with those of the micrograph.

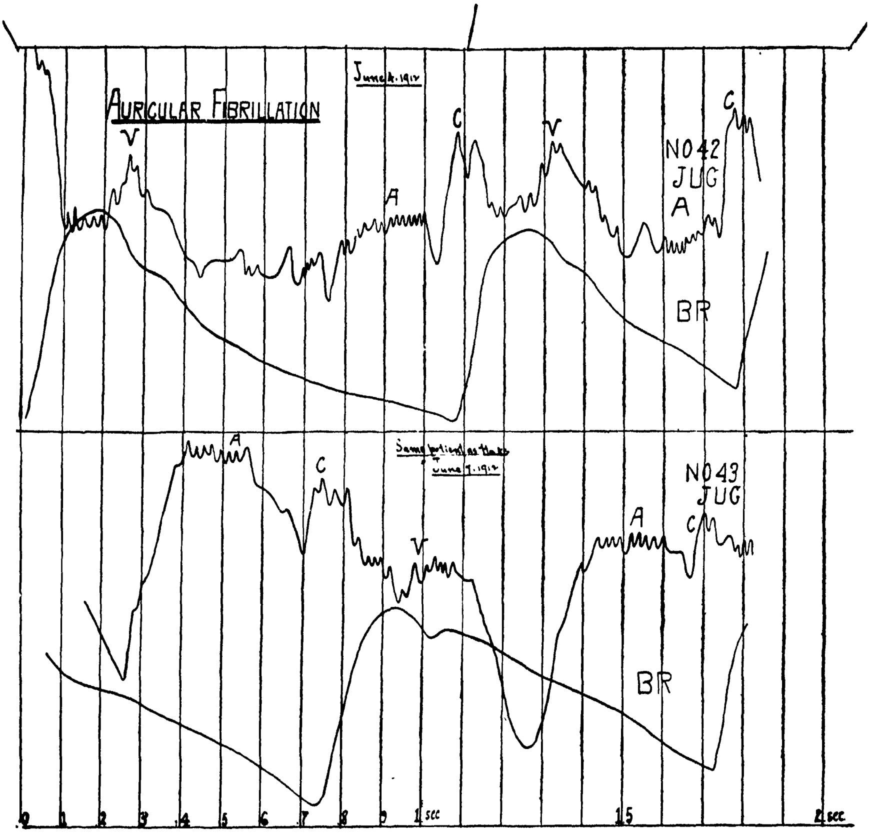


FIG. L.

There are certain curves marked especially in those of the apex vibrations as being A and B group. These, as was shown by Crehore, were produced by the closure in the A group of the auricular ventricular valves, and in the B group by the closure of aortic valves. In both the Jaquet and in the micrograph the M wave between the A and C waves comes out particularly clearly and in both sides of curves the H wave also is more noticeable than in the usual polygraphic curves.

In the micrographic curves also marked No. 92, Fig. K, there is shown a distinct alternation of the brachial pulse.

In Nos. 42, 43 (Fig. L), 134 and 135 (Fig. M) the auricular fibrillation is very clearly seen showing the vibratory character of the waves transmitted to the jugular vein, and also the lack of any definite or auricular

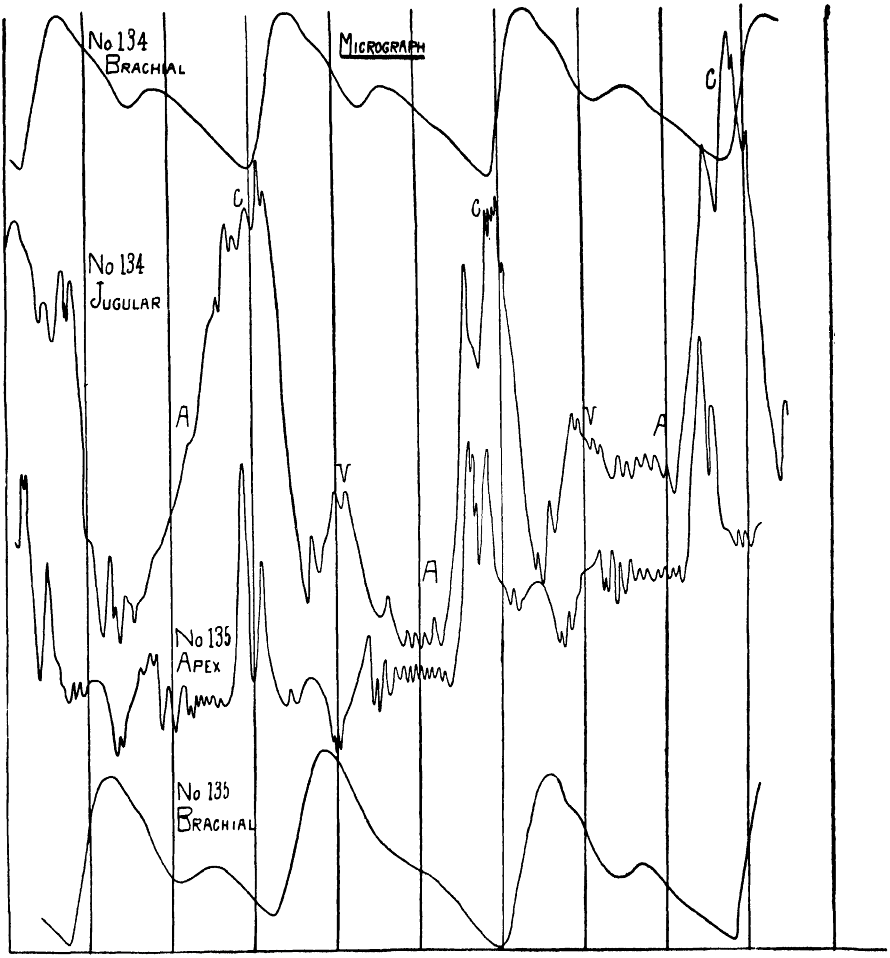


FIG. M.

curve in some instances, and again the vibrations occurring on such a wave even when there is a definite contraction shown, sufficient to transmit an impulse through to the ventricle and produce a C wave.

In No. 129 (Fig. N) there is well shown a graphic picture of an aneurysmal thrill during diastole between the closure of the aortic and the auricular ventricular valves.

In No. 135 (Fig. M) in the apex beat there is very clearly shown the vibrations produced by a presystolic murmur.

Because of their spacing by lines instead of the regular notching of the time marker, these curves show more clearly the relations of the venous to the brachial and radial curves.

Electrocardiograms.—In considering the electrocardiograph instrument it is unnecessary to discuss the theoretical construction of the machine or the details of its manipulation. These can be obtained from books of electrical cardiographs and books especially devoted to that study. Suffice it to repeat that the current passes through the galvanometer string set between two magnets, the string moves at right angles to the current in the magnet. The record of the string is not the record of the force of the heart contraction. The deflection of the string is simply the record of the difference of the potential between the two electrodes, and this is proportional to the space of time which elapses while

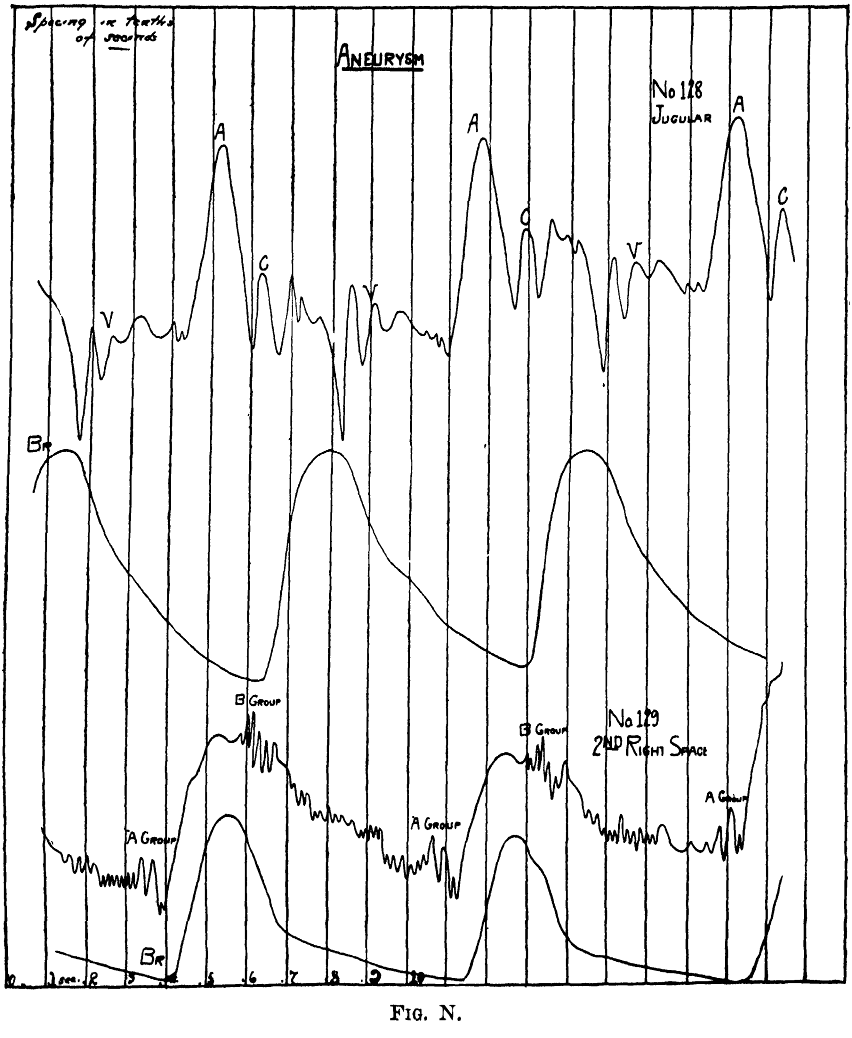


FIG. N.

the current passes from one electrode to the other. The deflections of the string are also greater or smaller in proportion to its state of tension and for this reason the string and its tension are standardized before taking the electrocardiogram so that a millivolt of current will cause the string to move a centimeter in front of the camera slit.

The normal electrocardiogram is divided into two parts; the auricular complex which is the rise of the wave P and from there to the occurrences of the Q wave, which is the beginning of the ventricular complex. If Q be absent the beginning of the R shows the end of the auricular complex. The PR distance marks the length of time the impulse takes to travel from auricle to ventricle, it is the AV interval. The ventricular complex starts from the beginning of Q or R and goes to the end of the wave T, that is, it is spoken of as the deflection QRST. These letters were originally introduced by Einthoven and are retained because they do not attempt to indicate the cause of the deflection and are purely arbitrary. These deflections occur before contraction in the heart of any chamber of the heart. There is a discussion whether or not the T wave is produced by the contraction or by the fact that the excitation lasts longer at the base than at the apex. The true explanation seems to be that the T wave is caused by the passing away of the excitory process and not by the contraction of the ventricle.

It is always to be remembered, as has already been stated, that the electrocardiogram obtained from the normal heart is really a bigram or the algebraic sum of the impulse going down the left bundle (the levigram) and the impulse going down the right bundle (the dextrogram). By studying the variations of the two curves the final share which each ventricle plays in the production of the QRS complexes has been obtained. These differences in the normal complex do not refer to the T part of the ventricular curve because this occurs so late in systole that the excitation wave has had a chance to spread through the muscle of the heart even if either branch of the bundle be damaged.

Method of Making Electrocardiograms.—Electrocardiograms are taken from three leads. For the purpose of taking an electrocardiogram the electrodes are placed on the right and left wrist or the hands placed in solutions and the electrode on the left leg or the left foot placed in the solution. In the first lead the current goes from the right to the left arm, in the second lead from the right arm to the left leg; and in the third lead from the left arm to the left leg. These are the standard leads; for it is known that if the wave pursues an abnormal course through the heart it will produce an abnormal electrocardiogram and if the points of contact which the instrument makes in the body are altered the curves are altered correspondingly. These standard leads, therefore, are always used in taking an electrocardiogram so that any variations may be due to variations in the heart, and not from the position of the electrodes.

Interpreting Electrocardiograms.—The curves taken from any two individuals are not exactly alike, but by experience the limits of variation compatible with health have been ascertained. In normal physiologic curves the auricular wave P is directed upward as a summit in all leads. It is small and rarely exceeds two scale lines in height. It is followed by a short line which is horizontal or tipped towards R. Occasionally P may be inverted in the third lead. Auricular complexes of these forms express the origin of the heart beat at the normal site of impulse formation and the passage of the wave through supposedly the whole of the auricular tissue in definite directions. The physiologic type of the ventricular complex shows a wider variation than the auricular. R and T are always present, but Q and S may be absent. All the deflections vary in amplitude and shape, and T in certain leads may normally vary in its direction. The total duration of the QRS group of deflections in normal subjects is no more than one-tenth of a second, and the presence of the QRS group followed by a slow, blunt T deflection shows that the ventricular contraction has been propagated from normal points, and has been awakened by impulses which should traverse the auriculoventricular bundle, its main divisions and their arborizations.

Electrocardiographic curves are modified in general by age. The chief change is a decrease in the amplitude of T as the subject becomes older. The curves are also modified by displacement of the heart and they are modified also by exercise, notably in the direction of an increase in the amplitude of T. The same subject gives curves identical in form from time to time. This is so pronounced that the identity of an individual coming in under different names in the hospitals has been recognized by his electrocardiograms.

One must always remember that an electrocardiogram may be normal in form but it does not follow that the heart is normal. It simply means that the impulses arise normally and proceed normally in their spread. If, however, electrocardiograms show notable divergence from the normal, it is highly probable that the heart is abnormal. In general, it can be said of the different leads than in Lead I, Q is a right ventricular event, R is mainly a left ventricular event, S is a right ventricular event. In Lead III, Q is a left ventricular event. To summarize the complexes in normal electrocardiograms in the three leads, one can say that P in normal subjects is always upright in Leads I and II, but P may be inverted in Lead III without necessarily implying an ectopic contraction. Deflections R and T are always present, Q and S may be absent. R is always directed upwards and is normally most prominent in Lead II. Q and S are directed downwards. In healthy individuals T is always upright in Lead II, usually so in Lead I, but may be inverted in Lead III and when inverted in Lead III it is usually accompanied by notched or bizarre QRS group. The inversion of T in Lead II is always pathological, sometimes also in Lead I. This inversion in Lead II is also of bad prognostic significance. Sometimes normal electrocardiograms exhibit notches in R and S. In Lead III the bizarre types are not uncommon. In normal subjects the QRS group does not exceed one-tenth of a second and the normal PR interval varies from .12 to .18. It never exceeds .2 seconds in health; that is, the limit of the normal PR interval is one-fifth of a second. There is a deflection U occurring in some curves during the period of diastole and it may be prominent. Our knowledge concerning it does not seem to extend beyond the fact of its occurrence.

Figure I is the curve of a normal heart. The PR interval is less than two-fifths of a second. The QRS is of normal value and the T follows regularly. The R is the highest in the second lead and it shows the curious notching in the R wave with the inversion of the T in the third lead that comes in some normal people.

Figure II also is a normal curve and shows the notching of the P wave with the inversion of the T that occasionally occurs.

Figure III is an electrocardiogram of a true dextrocardia, and shows the difference of the curve when the heart is transposed to the right side of the body instead of being in its normal position. The inversion of the waves in the first two leads is an interesting contrast to the normal position.

Figure IV is a curve of a heart which was on the right of the median line of the chest and had been drawn over into the cavity produced by the contraction of the middle and lower lobe of the right lung, following an empyema. The inversion of the T and P in the first lead is similar to the dextrocardia, and the R wave is longer than in the second lead. The R wave corresponds to the S wave of the dextrocardia curve in the second lead, the curves, however, are normal except the T wave is excessively high. The third lead is interesting, showing an equal size to the R and S waves.

There are two conditions which the electrocardiograph shows which are not irregularities in the beat of the heart but show the preponderance of the right or left cardiac mass.

Figure V shows the right ventricular preponderance in which the first curve shows a small R and a long S and the third lead shows a high R giving one the impression as one looks at the curve as if the R waves turned in towards each other.

Figure VI is the left ventricular preponderance in which the S curve is prominent in the third lead. The comparison of the R and S curves in the first and third lead gives one the impression as if they turned out away from each other. The R curve in the first lead in this series and the S curve in the third lead show also a very distinct alternation. This corresponds to the pulsus alternans of the polygraph. These conditions of right and left ventricular preponderance occur in hearts in which for any reason the right or left ventricle is excessively hypertrophied and preponderates over the normal mass. This would occur in lesions of the valves of the right heart, as in times of mitral stenosis, or in the left ventricle accompanies the lesions of the valves. But if the whole heart is hypertrophied in both right and left sides, even in very large hearts there are in some cases but slight signs of one side predominating over the other, as far as the electrocardiogram is concerned.

Figure VII is a case of premature auricular contractions. This is shown in the third lead and the fourth beat from the left and again at the eighth beat. The P wave is sunk here in the preceding T wave but it is evident that the impulse comes from a supraventricular origin as the ventricular complex, the RST waves are normal. The impulse therefore has come down from the auricle to the ventricle in the normal path and the ventricle has responded with the contraction. The pause following the contraction is longer than the regular rhythm. In this curve there is also the left ventricular preponderance.

Figure VIII shows the auricular ectopic beat with the inverted P, the impulse starting from a point in the auricle outside of the sinus.

That there may be at the same time auricular extra systoles and ventricular extra systoles is shown in Fig. IX, in which in the first lead the first three beats are out of time with the rest of the rhythm in that lead and in the second lead are extra auricular systoles and in the sixth beat from the left where the P wave is sunken in the previous T. In the third lead the last beat is a right sided ventricular extra systole as it has no corresponding P wave and is an abnormal ventricular complex; the R points upward showing it to be a right ventricular event. The P wave in the second lead is upright showing that the ectopic focus was very near the sinus or it was a premature beat disturbing the rhythm from the sinus itself.

Figure X shows a simple tachycardia with the inversion of the P showing the rise from an ectopic auricular source and is really a succession of rapidly occurring ectopic beats in which a focus more rritable than the sinus has taken control of the rhythm of the heart.

Figure XI shows a paroxysmal tachycardia which has gone into the rhythm of the flutter giving a rapid irregular pulse. In the third lead on the fifth beat from the left there is a left ventricular ectopic beat.

Figure XII (a) shows a regular auricular flutter with a slow regular beating heart, in which the ventricle answers to every fourth beat of the auricle.

Figure XII (b) shows a heart in which the auricle is in flutter, but a few minutes later as in Figure XII (c) the ventricles are showing right and left ectopic beats.

When the auricular impulses lose the regular rhythm of the flutter, and become irregular, although the muscle contracts in rather large masses but irregularly, it amounts practically to the same condition as an auricular fibrillation in which there is too rapid an auricular contraction and the muscle vibrations are in such constant irregular state of refractory irritability that the contraction impulse is constantly blocked in its passage from the auricle to the ventricle and there is in the curves the irregular, coarse, wavy picture as seen in the third lead of Figure XIII as a rapidly beating heart with auricular fibrillation in which the auricular waves are shown with complete irregularity and there is equally complete irregularity of the ventricle response. This condition of the auricles can occur whether or not the heart is beating rapidly or slow.

Figure XIV shows an auricular fibrillation in an infrequently beating heart.

Figure XV shows the occurrence of an auricular fibrillation in which the fibrillation occurs in paroxysm and is not a constant feature in the heart. The first two leads show the variation at times between a coarse impure flutter and the irregularity of an auricular fibrillation and in the third lead this condition has ceased and the ventricle is responding to regular occurring rhythm from a normal auricular contraction.

Figure XVI shows an auricular fibrillation with a paroxysm of tachycardia originating in the right ventricle.

Figure XVII (a) and (b) show an auricular fibrillation with two right-sided extra systoles in the last beats of the second lead. The same heart in an examination a few minutes later showed a paroxysmal tachcardia. This tachycardia, however, was of ventricular origin and was not confined to either ventricle but is shown (XVII (b)) to proceed from alternating right and left ventricular beats.

Considering next the curves showing a simple blocking of an impulse on its way from the sinus auricular node to the ventricle even when arising normally from the sinus node:

Figure XVIII is the curve of a sinus arrhythmia; the spacing between beats is the only deviation from the usual normal curve. This shows where the blocking occurs in the sinus itself, and for some unknown reason it fails to transmit rhythmically its impulse processes. Lead I shows at the beginning and at the end of the lead, a temporary cessation of rhythm and in Lead II the rhythm is interrupted in the middle of the beats here given. In Lead III this peculiarity fails to appear when this lead was being taken.

In Fig. XIX there is shown a regular rate of cardiac beat in which the impulse coming from the sinus is blocked at the auricular ventricular node and is delayed in its passage down the bundle to cause the regular ventricular contraction. In other words the PR interval is prolonged to twelve twenty-fifths of a second the normal being five-twenty-fifths. As marked in the minute scale in the figure each minute scale represents one twenty-fifth of a second and the slightly heavier line corresponds to the fifths.

In Fig. XX there is an inconstant heart block and delayed conduction, at times the PR interval is normal as in the third beat in Lead I it is just one-fifth of a second. It is preceded, however, by a PR interval of three-fifths of a second and is followed by a P wave which fails to go through entirely and which again is followed by a P wave which goes through on time.

Figure XXI shows an inconstant retardation of the impulse in the auricular ventricular bundle and a two to one complete block. The heart is beating irregularly and with the inversion of the T's has the appearance that is given in digitalis poisoning.

Figure XXII shows the prolongation of the PR interval, and in which there are double and triple beats in which as in the middle group in the third lead is a regular beat followed by a left ventricular and a right ventricular ectopic beat.

Figure XXIII shows in the same heart the partial block followed regularly by right ventricular ectopic beats.

In Fig. XXIV (a and b) from two different patients, there is a complete heart block in which the auricular rhythm is running regularly and the ventricular is running regularly but the auricular and ventricular rhythms are completely dissociated.

Figure XXV is an example of nodal or auriculoventricular rhythm low down in the auricular ventricular tissue because the auricular contraction appears later than the ventricular and the impulse occurs at such a position that it causes the ventricular contraction slightly in advance of the auricular.

Figure XXVI shows premature beats in the nodal tissue of the auricular ventricular node. This causes a ventricular contraction without evidence of any auricular wave. The irregular rhythm is seen in the third beat of the first lead and the ninth, twelfth and fifteenth beats are caused by this occurrence; also the fifth beat of the third lead.

Figure XXVII shows a tachycardia produced by a series of rapidly recurring impulses taking place in the auricular ventricular tissue in which the P wave is shown following the R wave and notching the RT interval.

Figure XXVIII (a and b) are examples of right-sided ectopic beats; they show well the excessive height of the R wave and the reverse T wave.

Figure XXIX shows the left ventricular extra systoles. In the third lead the alternating beats show a P with an R, but a reverse T. The breadth of the R is but one-tenth of a second which is within normal limits while the extra systole from R to S shows a breadth of eight-tenths of a second; one-tenth of a second is the normal limit for the breadth of this wave.

Figure XXX (a and b) show ectopic beats of both ventricles from shifting foci in which the second beat of each pair is caused by a left ventricular extrasystole, and in the middle pair in the third lead there is also a prolongation of the PR interval.

Figure XXXI is a case of pulsus bigeminus in which the second beat of each pair is caused by a left ventricular extra systole and in the middle pair in the third lead is also a prolongation of the PR interval.

Figure XXXII shows a pulsus trigeminus in which the two extra beats are caused by the ectopic beats from the right ventricle.

Figure XXXIII is an example of a paroxysmal left ventricular tachycardia.

At times the cardiac impulse fails to go down either the right or left bundle branch of the conducting system; if the right bundle be blocked, it is believed that the electrocardiogram is a picture of the left bundle curve. That is, the curve is no longer the algebraic sum of a dextogram and a levogram, it remains the picture given as that of the transmission through only right or left bundle.

In Fig. XXXIV is given an example of the right bundle branch block, which shows a levogram or the picture that transmission through the left bundle alone will give.

In Fig. XXXV the left bundle branch block being given there is the picture of the transmission of the impulses through the right bundle alone.

Curves Taken with the Optical Capsule of Franck.—Through the courtesy of Dr. Wiggers, there are presented here some curves taken with the optical capsule of Franck. This instrument is a practical instrument for use in the ordinary work as it throws the light directly on a moving film and does not have to be transcribed from a film on to plotting paper as in the case of micrograph.

Figure XXXVI presents a curve in which the electrocardiographic second lead is compared with that of the jugular. A short run of six ectopic beats which is a short run of a paroxysmal tachycardia is shown and when compared with the jugular curve it shows some interesting phenomena.

In paroxysmal tachycardia of auricular origin there is a rapidly increasing strain thrown on the circulation and often the equilibrium of the circulation is rapidly disturbed and the heart does not empty itself. The jugular vein here seems to show a rapidly increasing reflux of blood with an increasing size of the A wave which ceases instantly when the tachycardia stops.

The tracings in this jugular curve show also the tracings nearer the true curves than those of the ordinary polygraph, as in Franck's instrument the faults of inertia are removed or reduced to a minimum. It also shows that in spite of accuracy in the delineation of the curves they do not give any more information than the cruder instruments with their faults of inertia. This jugular curve, however, shows also, if the interpretation here given is correct, an advantage which the electrocardiographic curve cannot give; it shows the increasing strain and disturbance of the circulation and indicates clearly that the polygraph has powers of showing changes in the peripheral circulation which the electrocardiograph can never possess.

The following two Figs., XXXVII and XXXVIII, show auricular fibrillation and the ventricular type of jugular curve. They show the comparison between the electrocardiographic curves in this arrhythmia and the polygraphic. They further show the occurrence as measured optically of the curve, due to the sounds as heard from the tonometer at the points marked 1 and 2 in the upper curve the first and second sounds occur and under the letters DII are indicated the vibratory sounds of a diastolic murmur. These are curves actually produced by sound waves.

Figure XXXIX shows a comparison in the case of complete block between the electrocardiograph and the optical curve of Franck; both curves are interesting; the two rhythms, the auricular and ventricular are disassociated, neither the auricular nor the ventricular is beating in a rhythm in which the beat is exactly equidistant. This makes the jugular curve peculiar in that every other A curve falls with the V curve.

The sound curve produced by the valvular closure in the heart is also interesting as showing clearly the difference between the first and the second sounds.

Figure XL shows the occurrence of the radial pulse just before the rise of the T wave.

In the electrocardiograph there is a slight irregularity in the ventricular rhythm, the contractions are not equidistant. This throws the P wave at various points on a curve in relation to the T wave. It also causes the same synchronous occurrences in the jugular curve of the A and V wave at every other beat.

No attempt has been made in describing these curves to discuss the origin or the meaning of their occurrence in relation to the functional or pathologic condition of the myocardium. They are evidences of disarrangement of the conducting system of the heart and as such show the injury which even the toxic poisoning or permanent destructive lesions produce in the conducting system in distinction from the contracting mass of the myocardium.

There is no question that the curves from the instruments here shown supplement each other. The polygraphic curves show more of the vigor and force still remaining in a damaged circulation or show the lack of vigor compared with a normal circulation, but it is only through the knowledge obtained by the electrocardiograph that arrhythmias may be at all times accurately differentiated.

We have no means at present of judging accurately the remaining vigor of a given myocardium or by comparing the physical signs with instrumental records judge how much vigor there remains in a failing heart. We have no instrument as yet which measures the force of a cardiac contraction.

There is no question, however, of the practical application and usefulness of these instruments and there is equally no question of the amount of knowledge and the ease with which it may be obtained by very little effort spent in studying the curves produced by these instruments. The knowledge obtained is easily acquired, the value of the reward received is out of all proportion to the necessary effort.

PLATE I

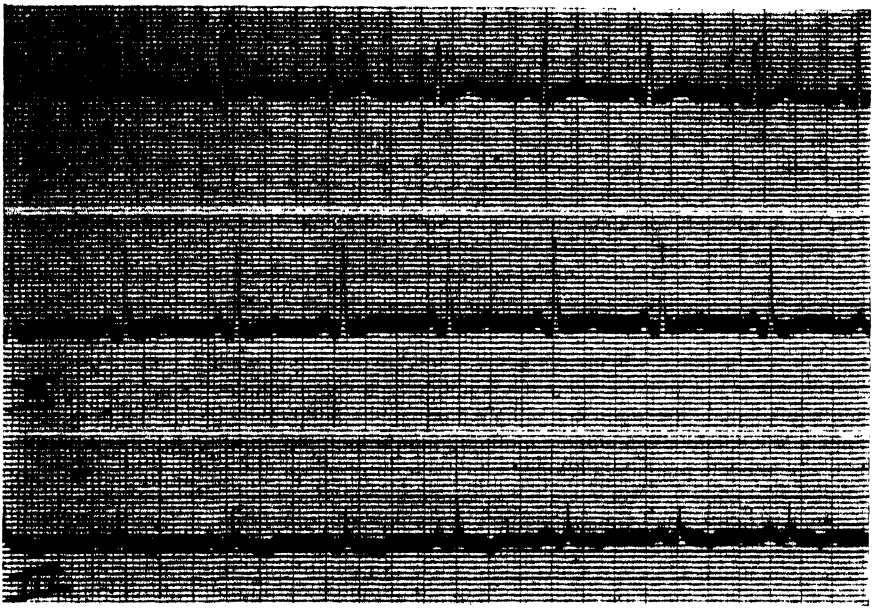


Fig. I.

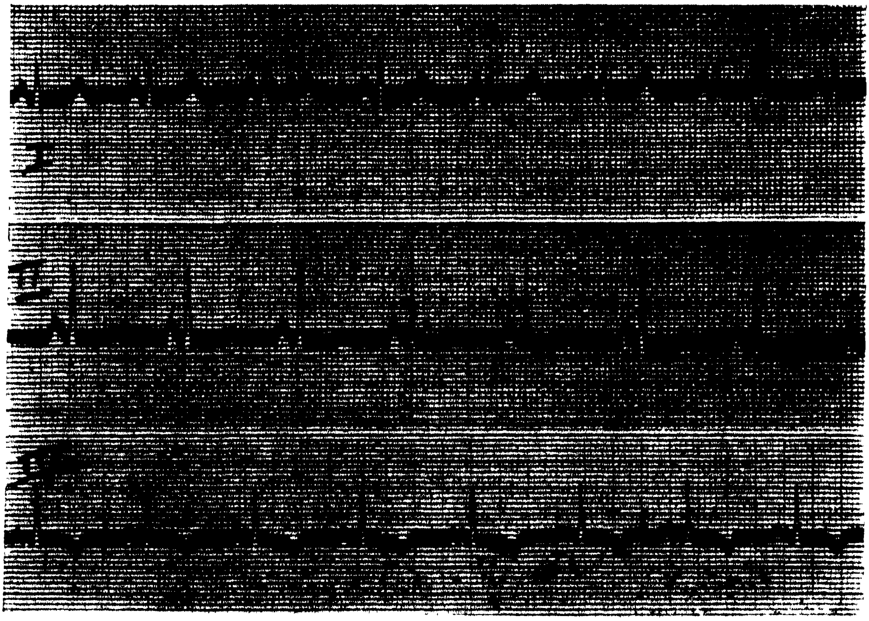


Fig. II.

PLATE II

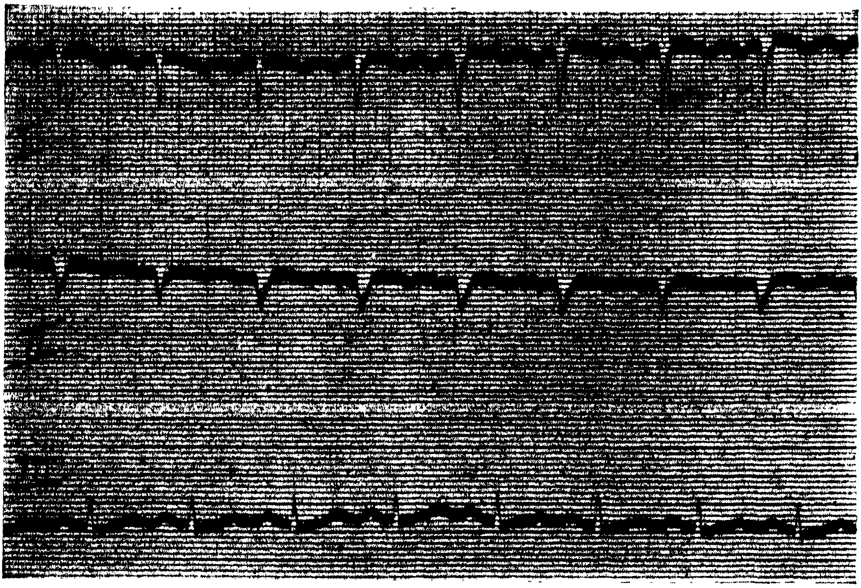


Fig. III.

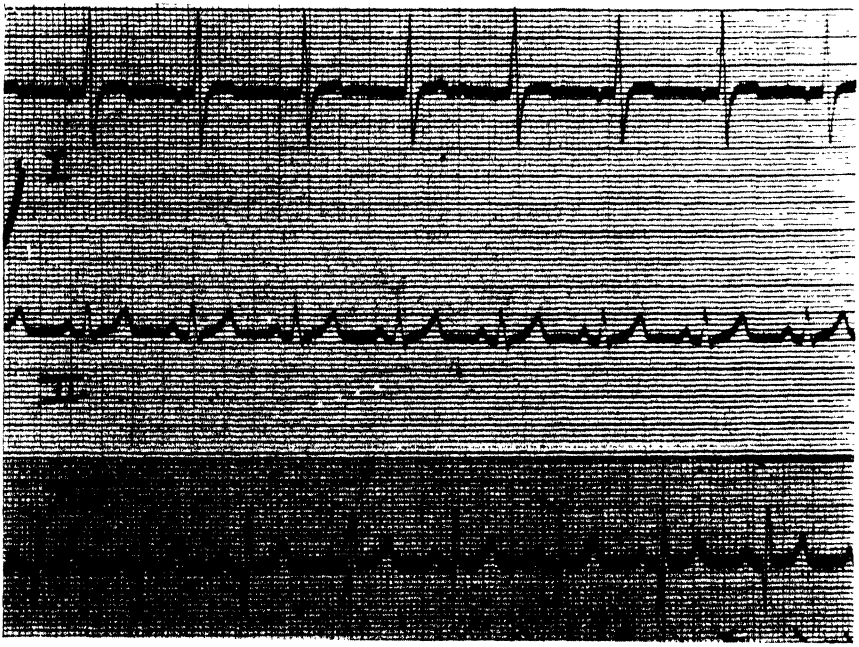


Fig. IV.

PLATE III

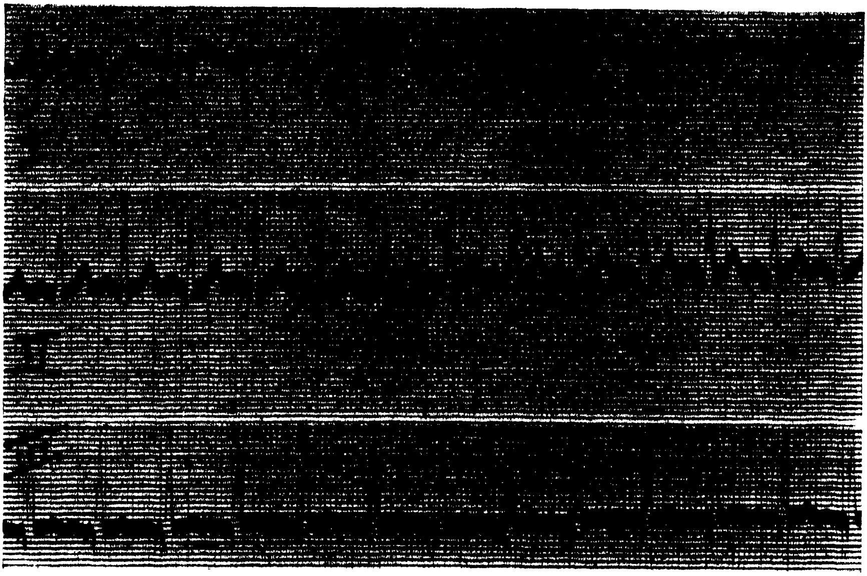


Fig. V.

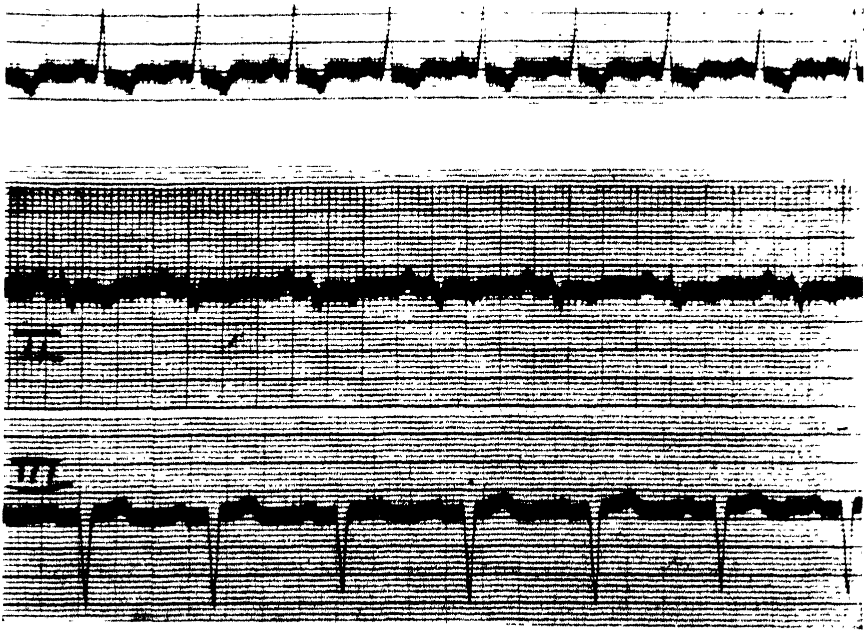


Fig. VI.

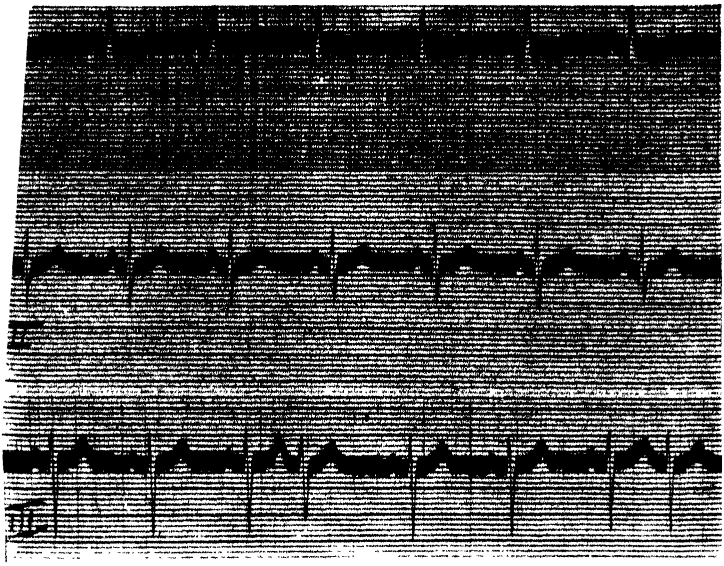


Fig. VII.

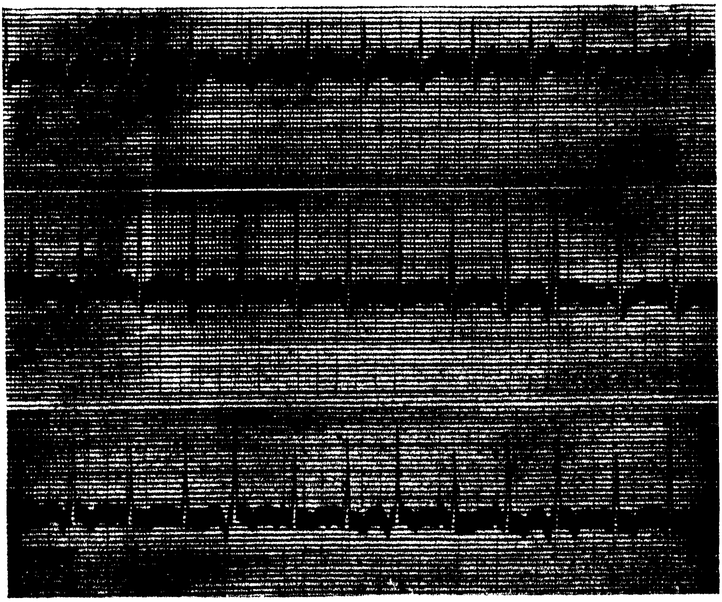


Fig. VIII.

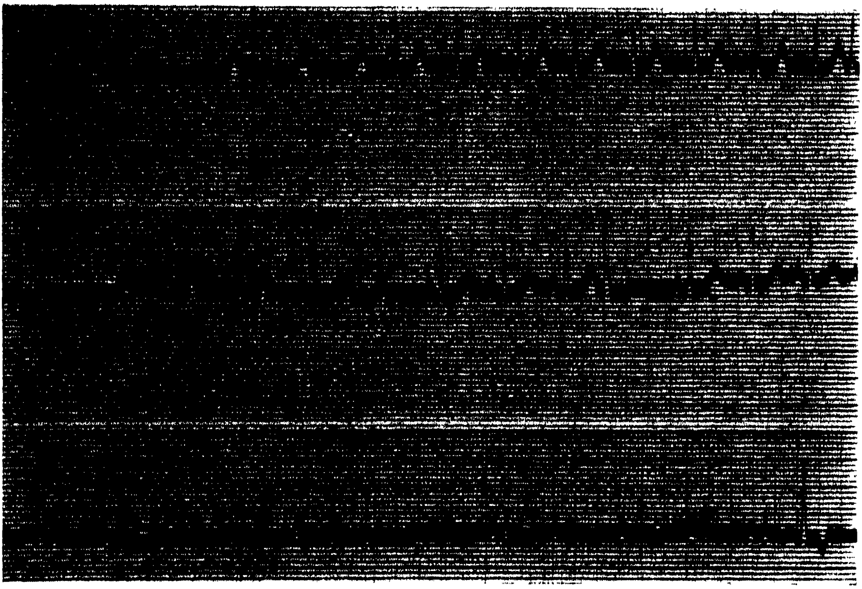


Fig. IX.

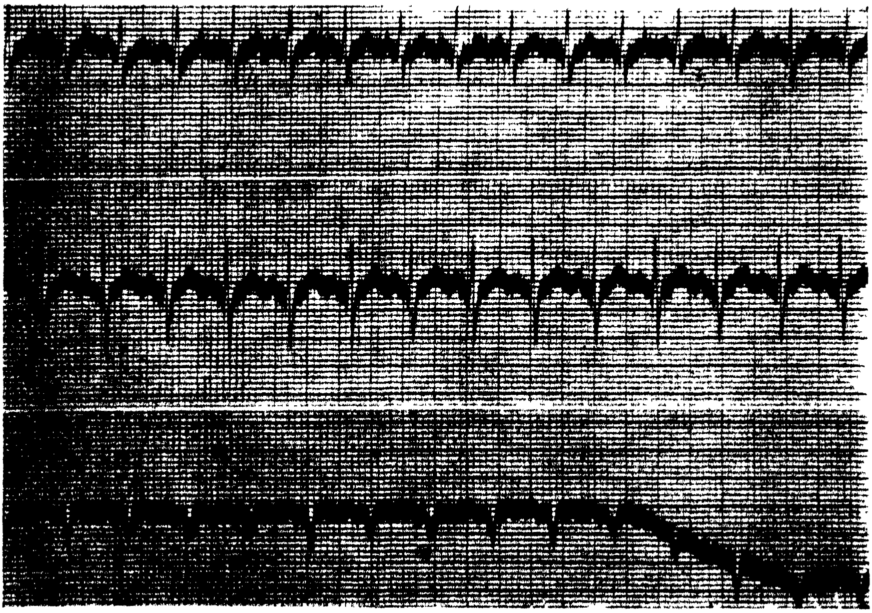


Fig. X.

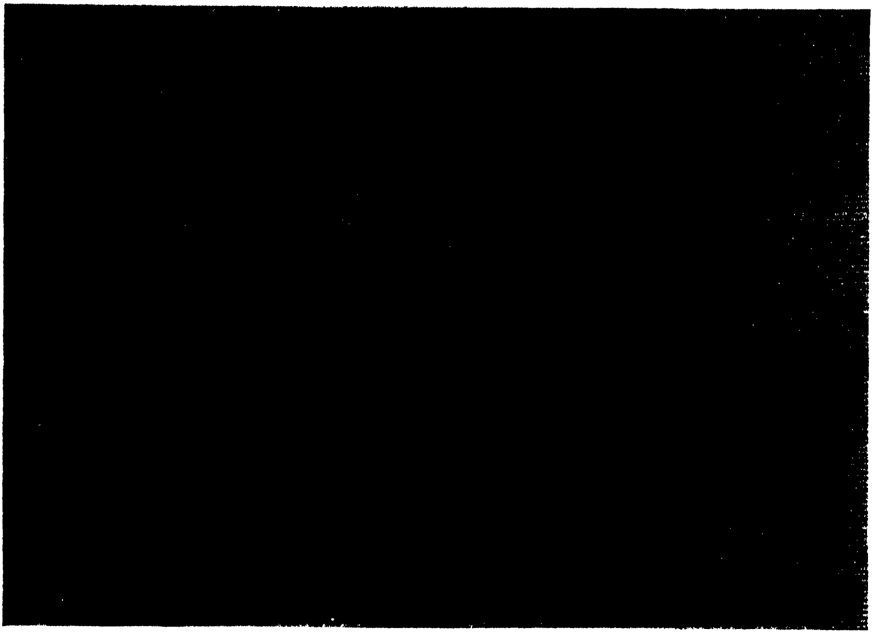


Fig. XI.

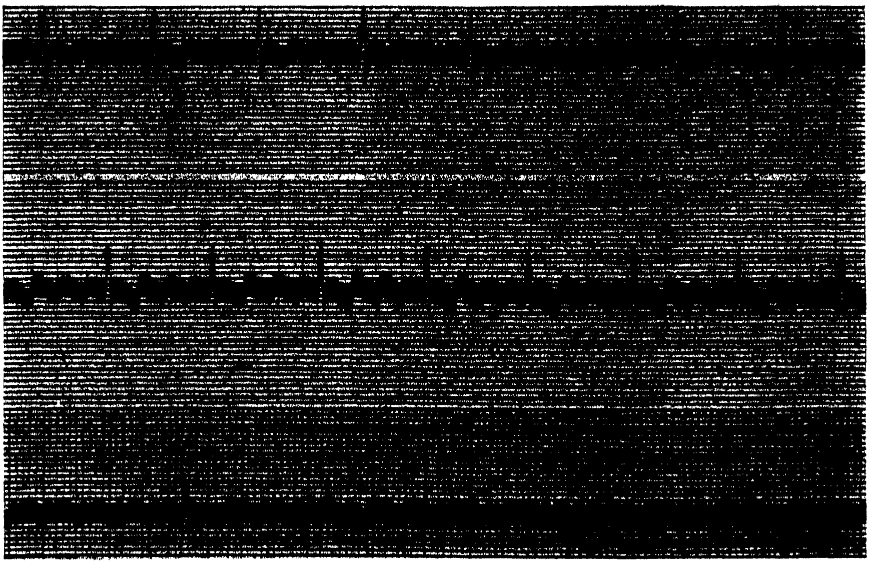


Fig. XII a.

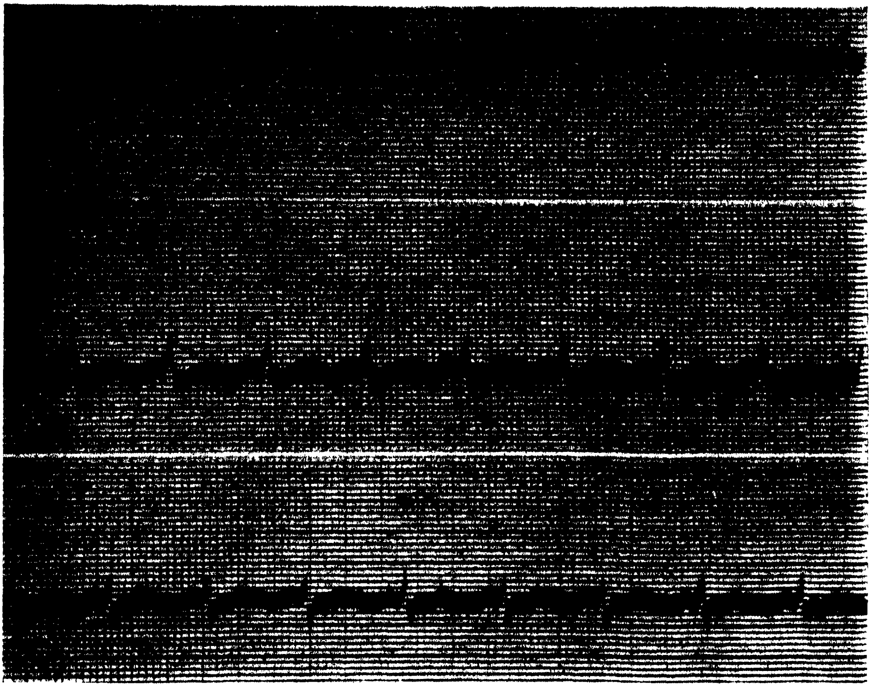


FIG. XII b.

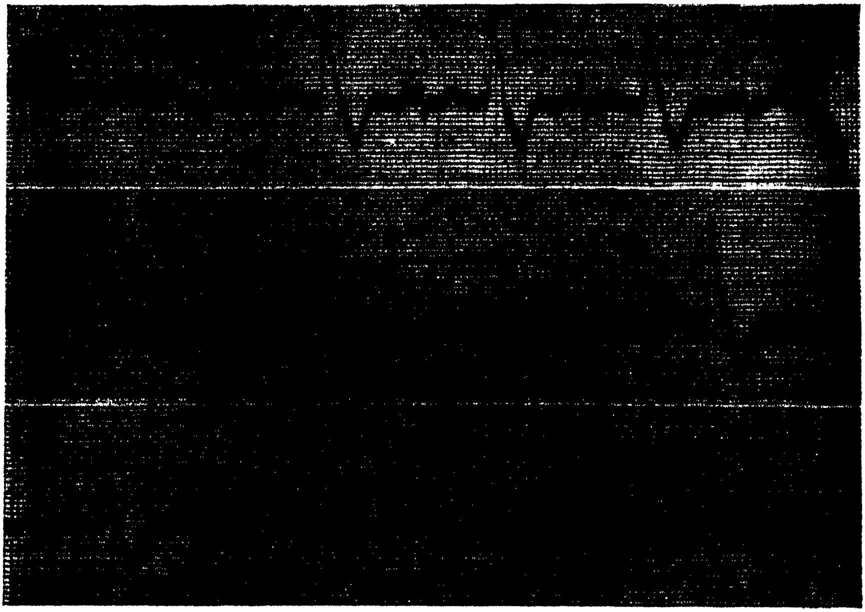


FIG. XII c.

PLATE VIII

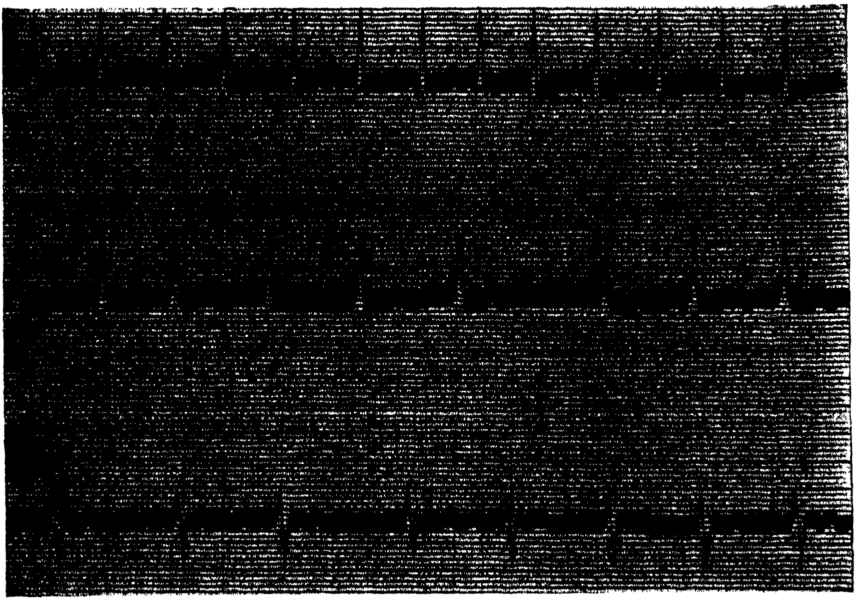


Fig. XIII.

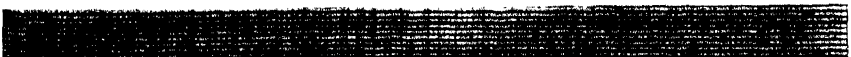


Fig. XIV.

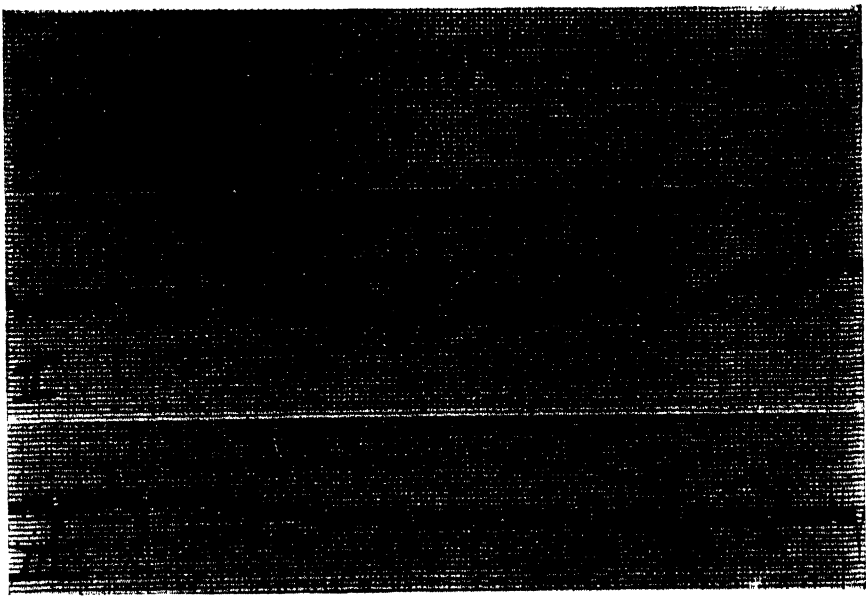


Fig. XV.

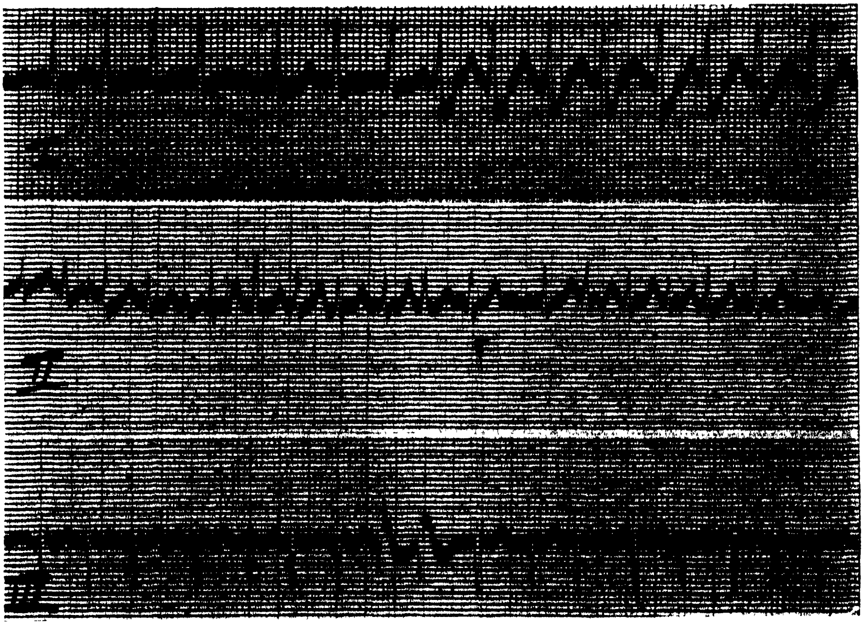


Fig. XVI.

PLATE X

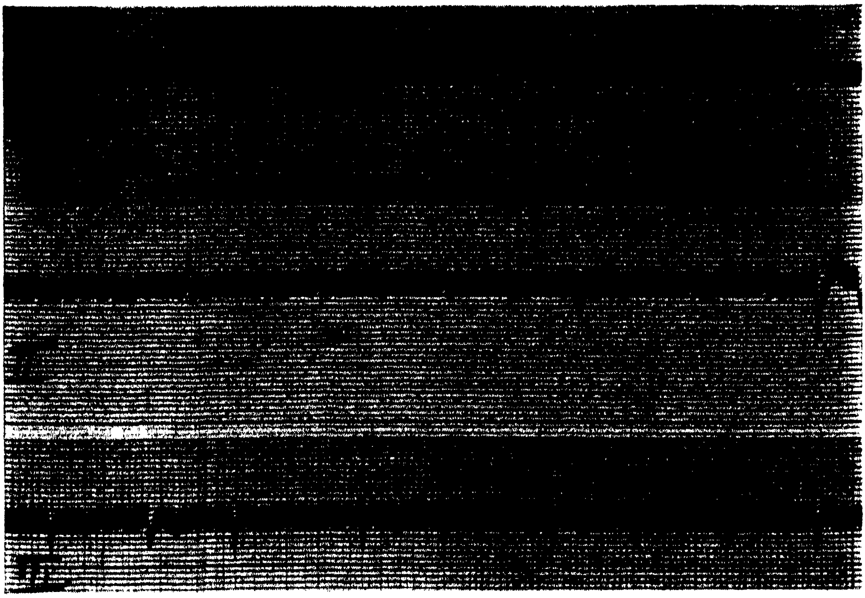


Fig. XVII a.

Fig. XVII b.

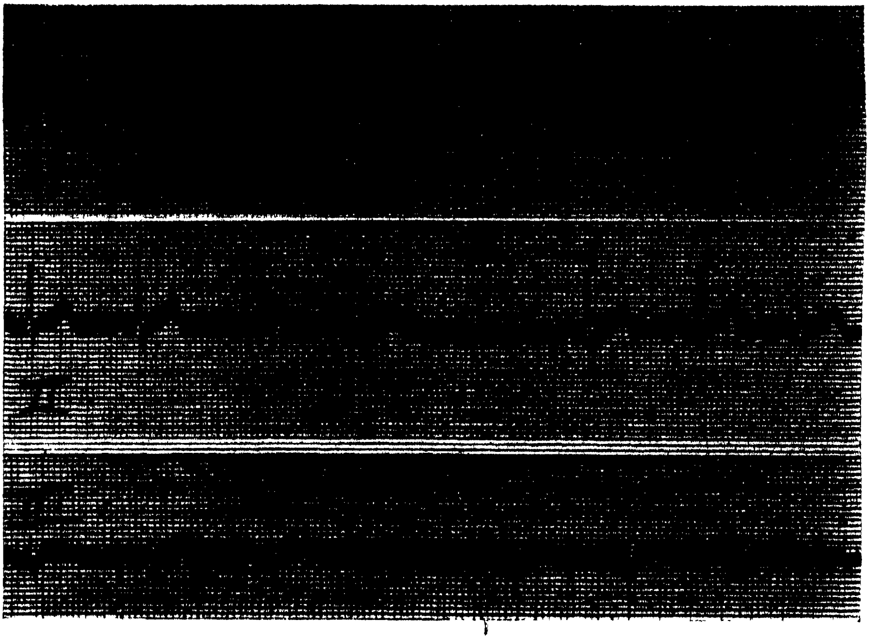


FIG. XVIII.

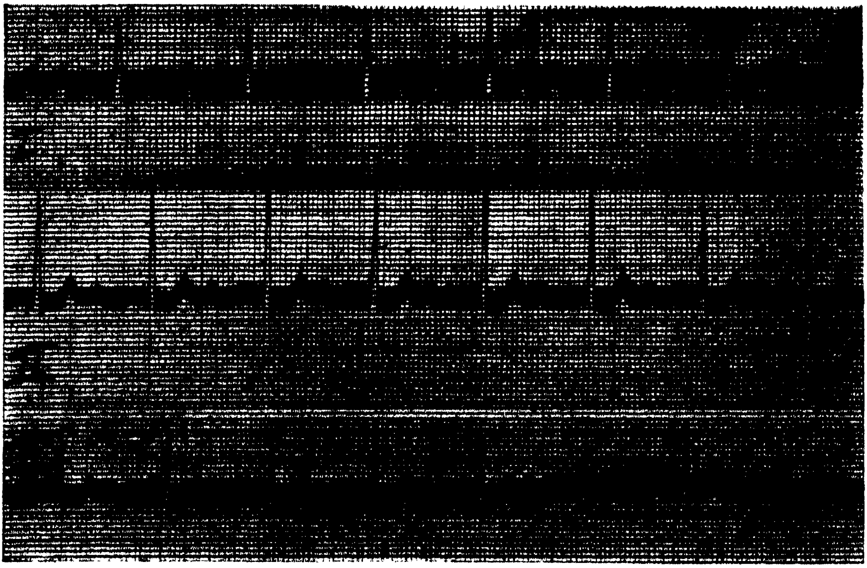


FIG. XIX.

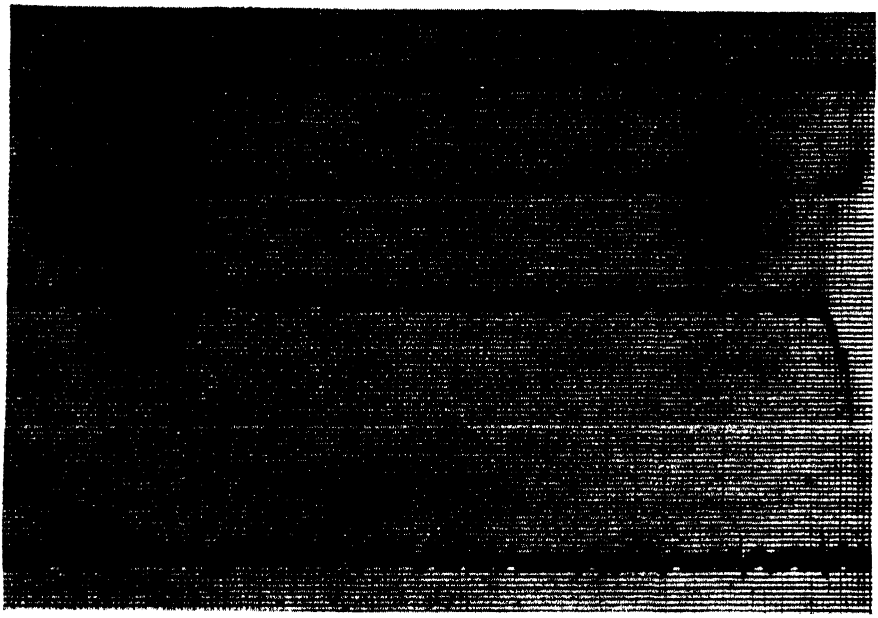


FIG. XX.

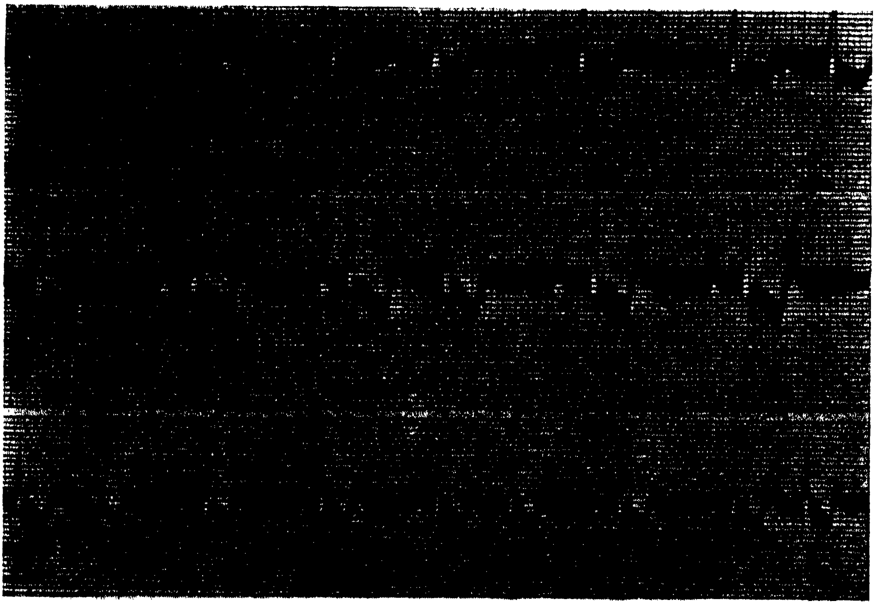


FIG. XXI.

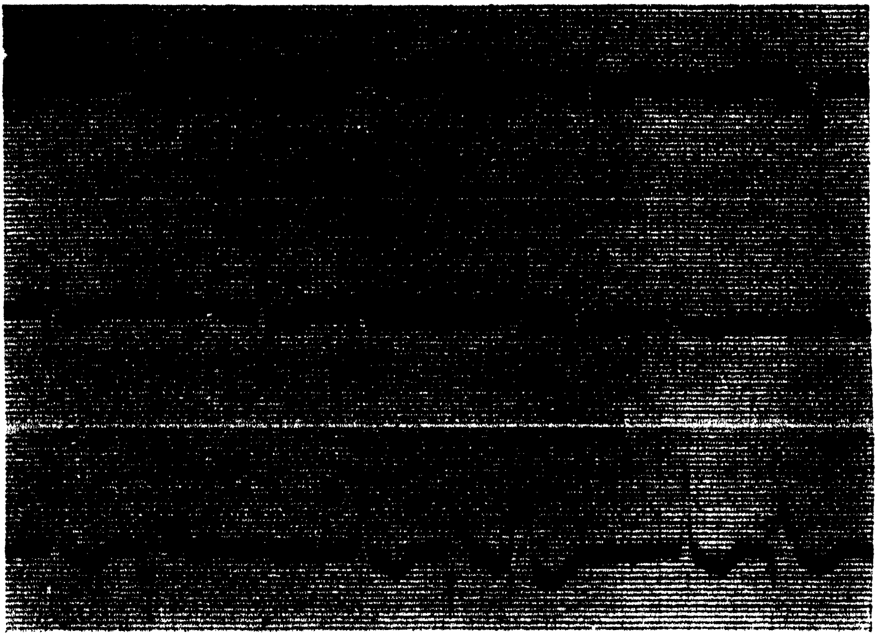


Fig. XXII.

Fig. XXIII.

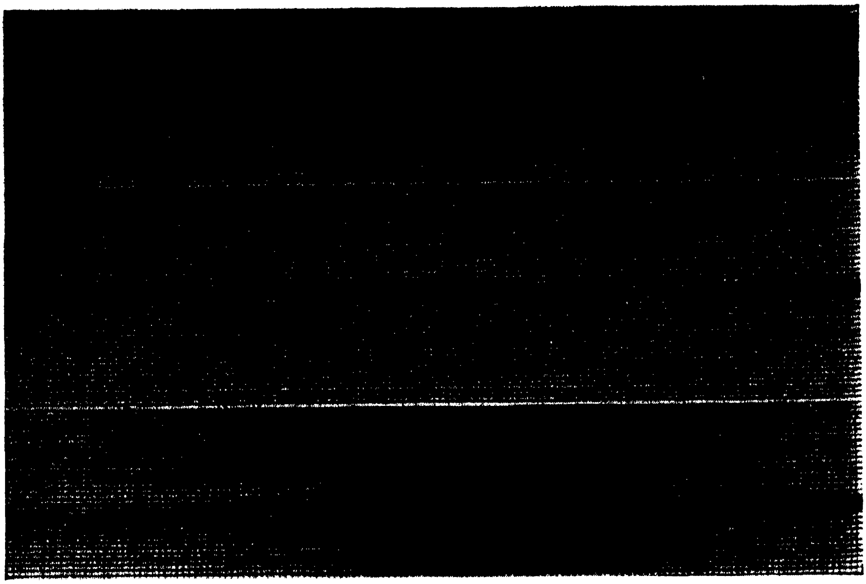


FIG. XXIV a.

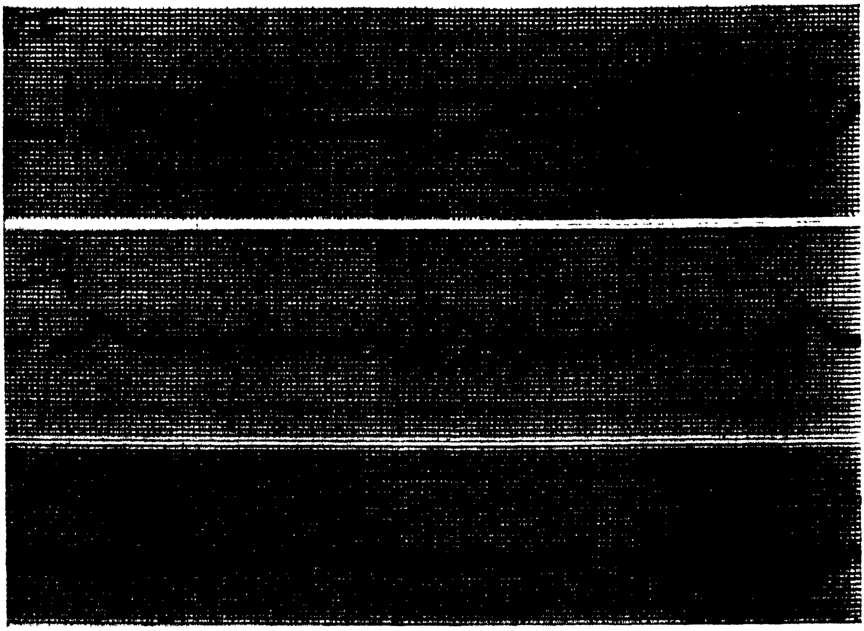


FIG. XXIV b.

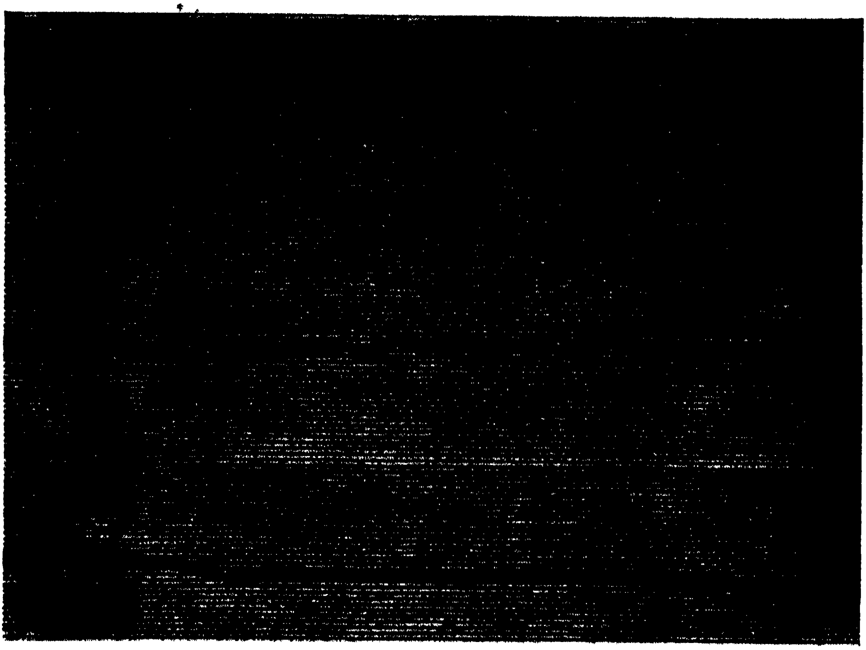


FIG. XXV.

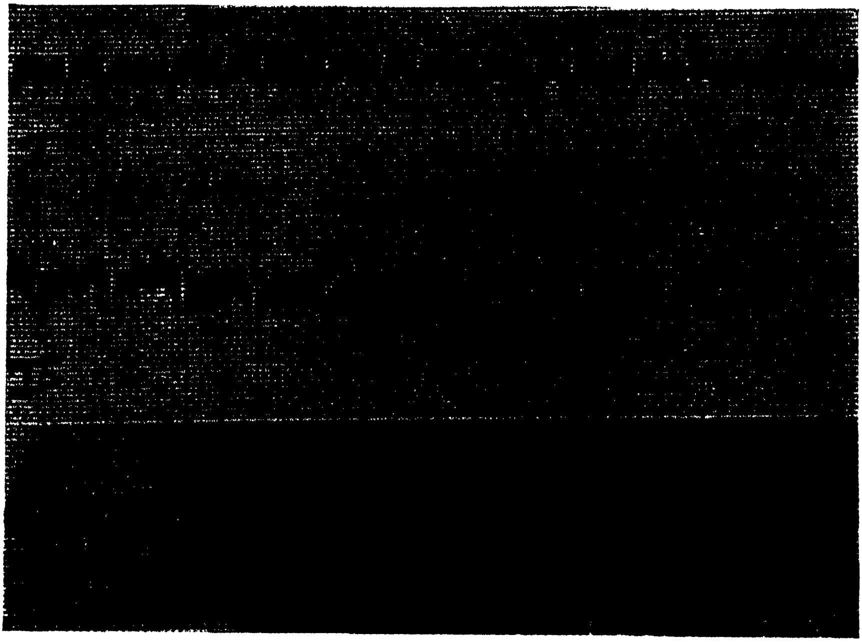


FIG. XXVI.

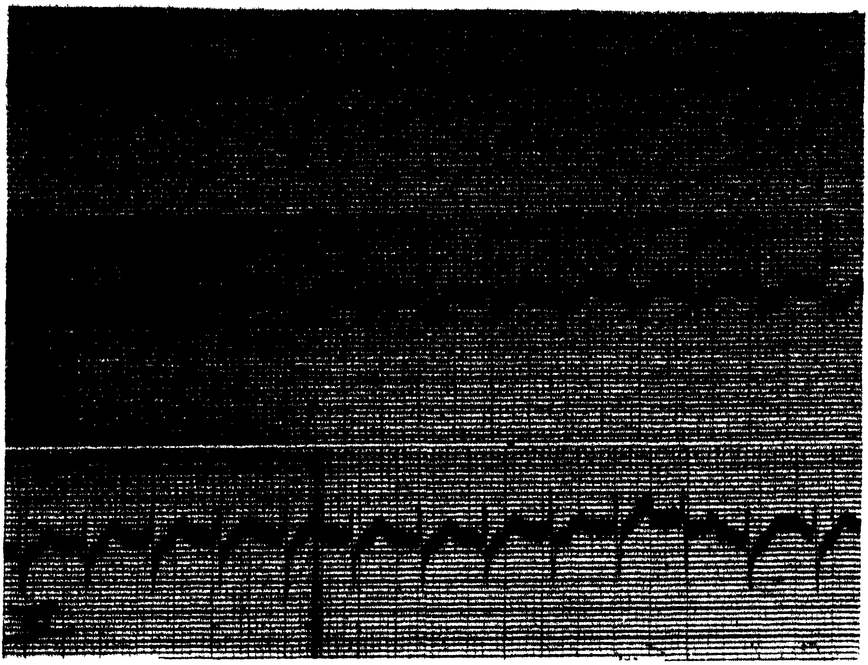


FIG XXVII.

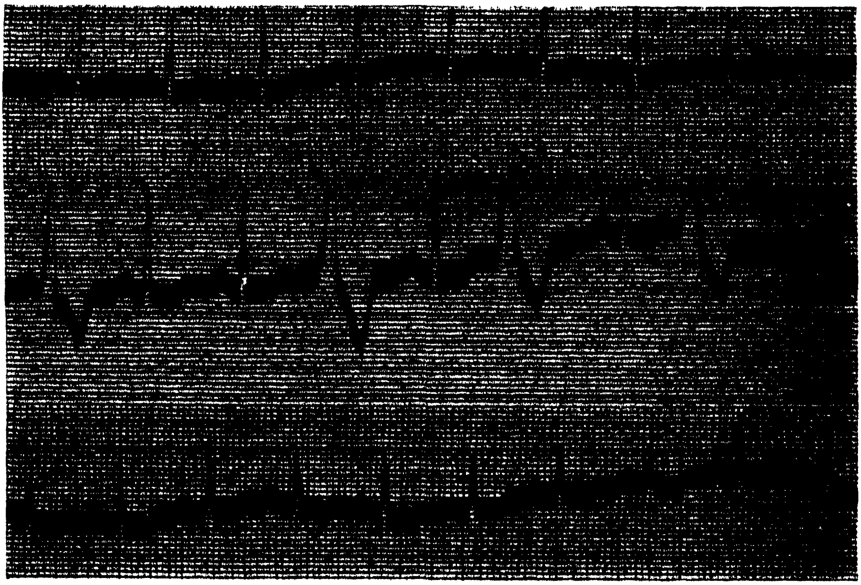


FIG. XXVIII a.

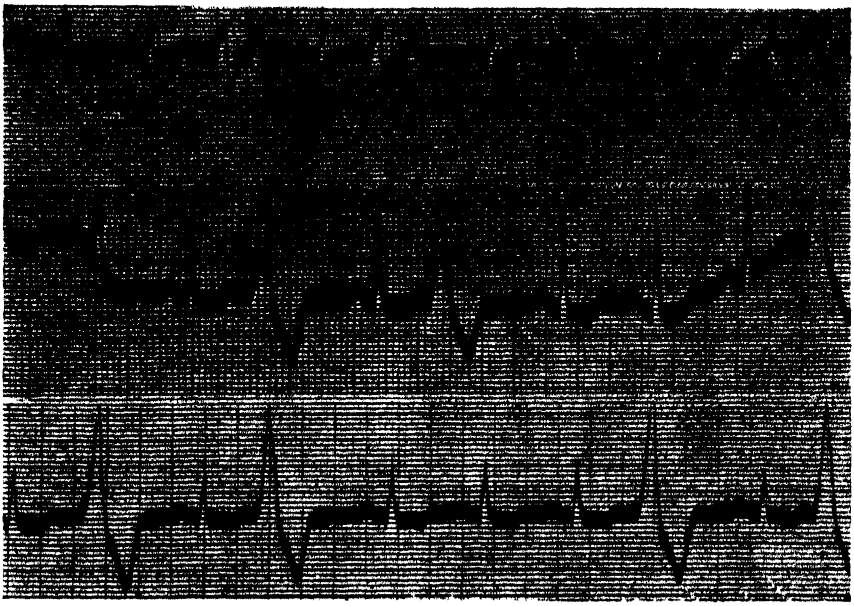
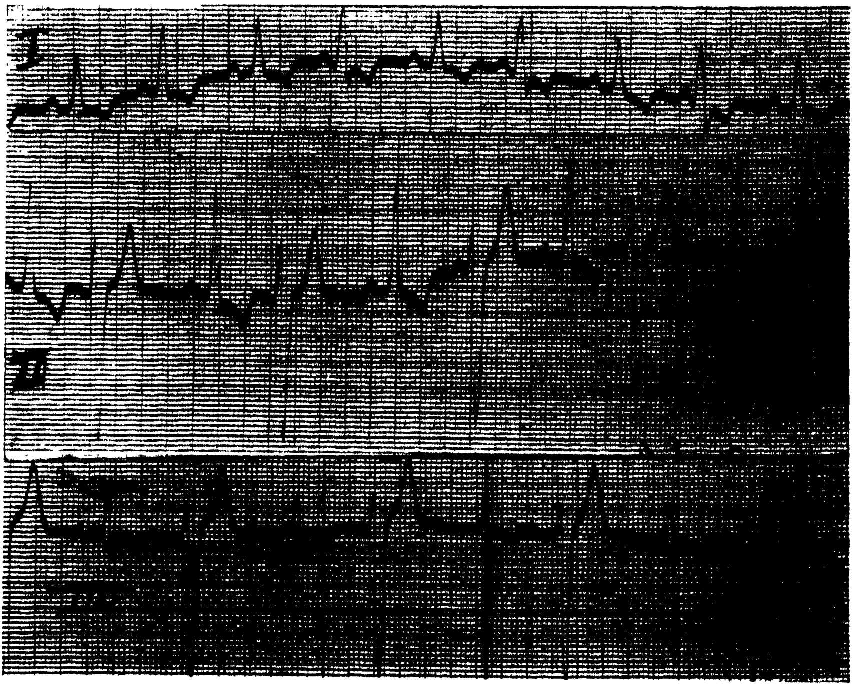


Fig. XXVIII b.



G. XXIX.

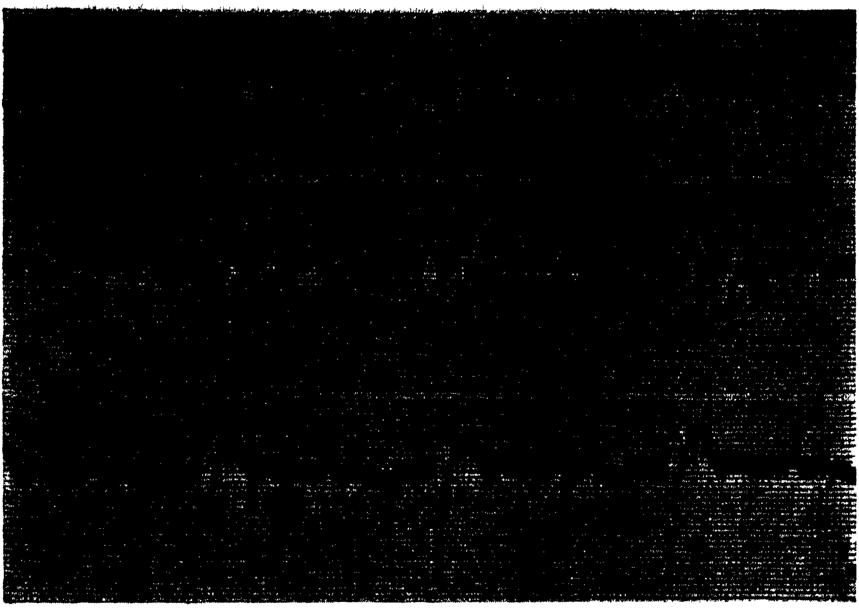


Fig XXX a.

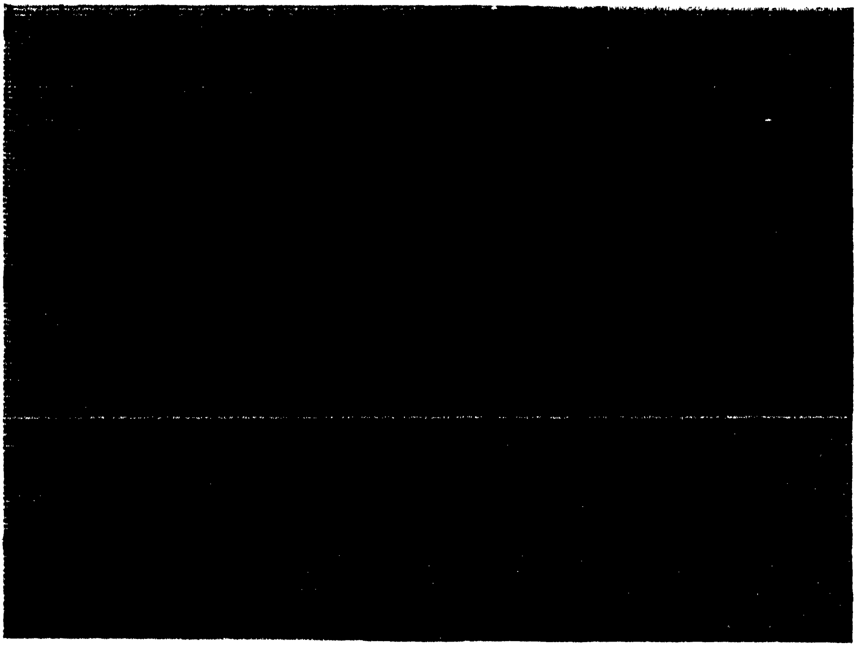


Fig. XXX b.

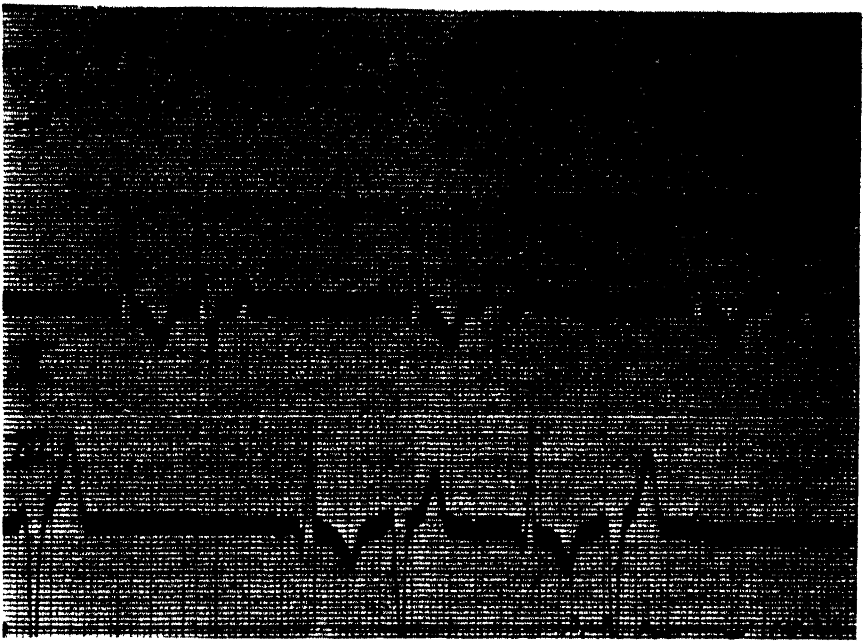


Fig. XXXI.

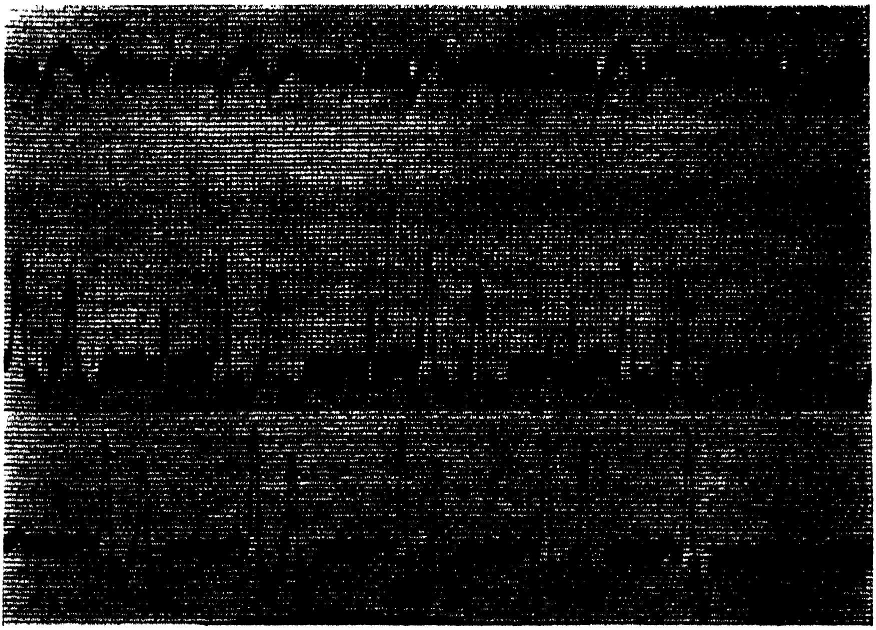


Fig. XXXII.

PLATE XX

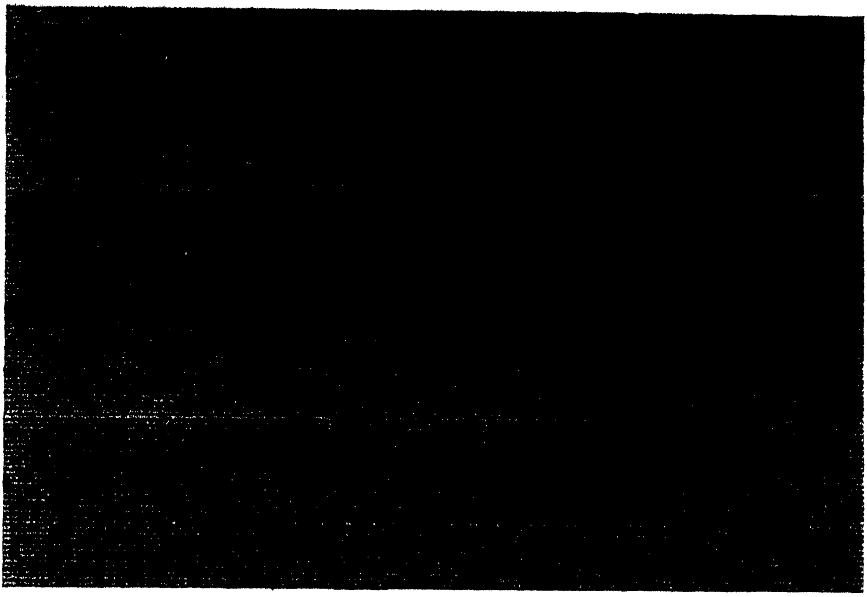


FIG. XXXIII.

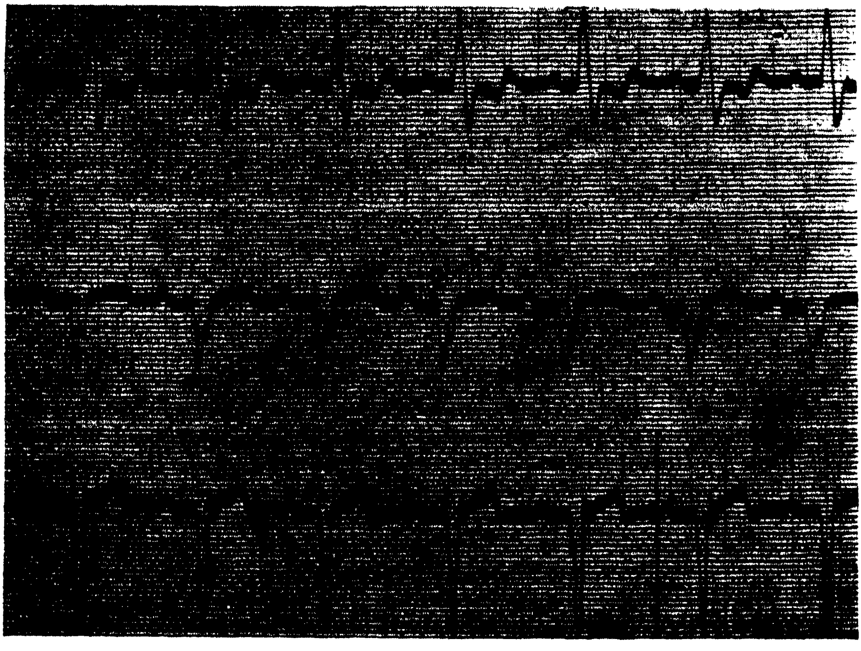


FIG. XXXIV.

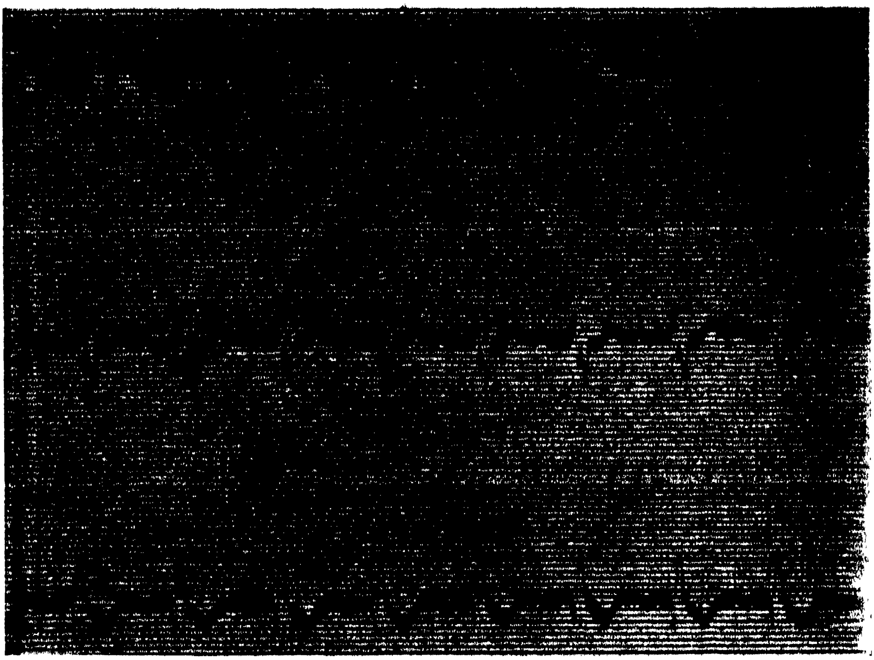


FIG. XXXV.

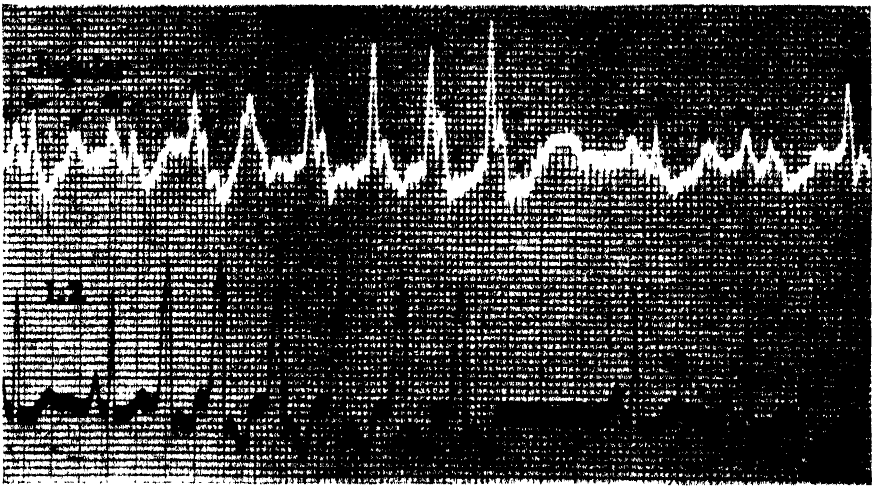


FIG. XXXVI.

PLATE XXII

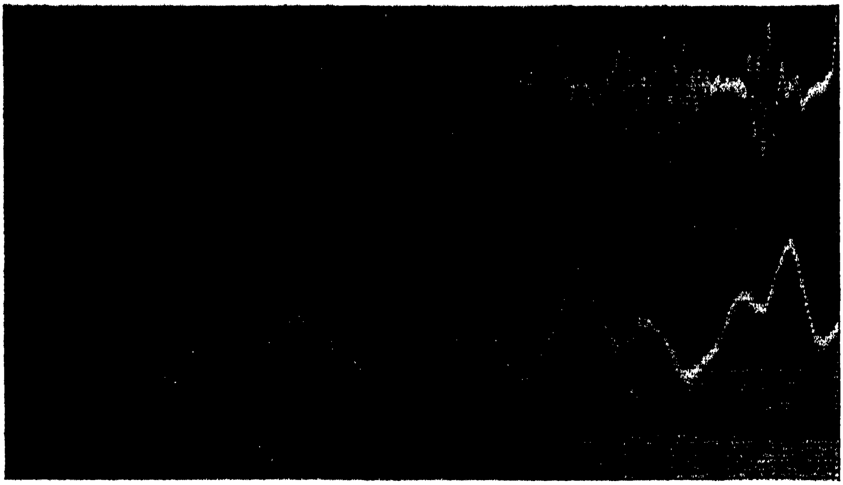


Fig. XXXVII.

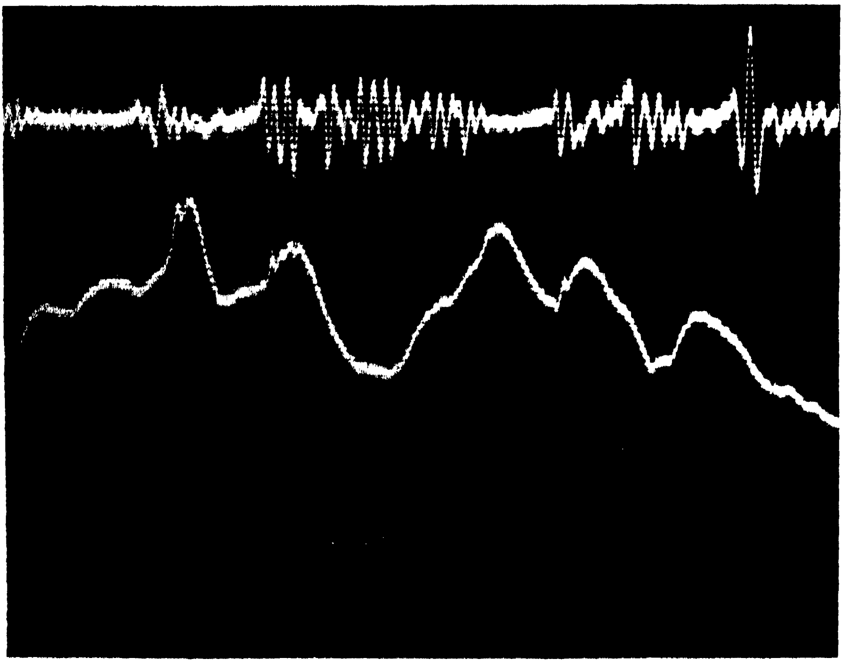


Fig. XXXVIII.

PLATE XXIII

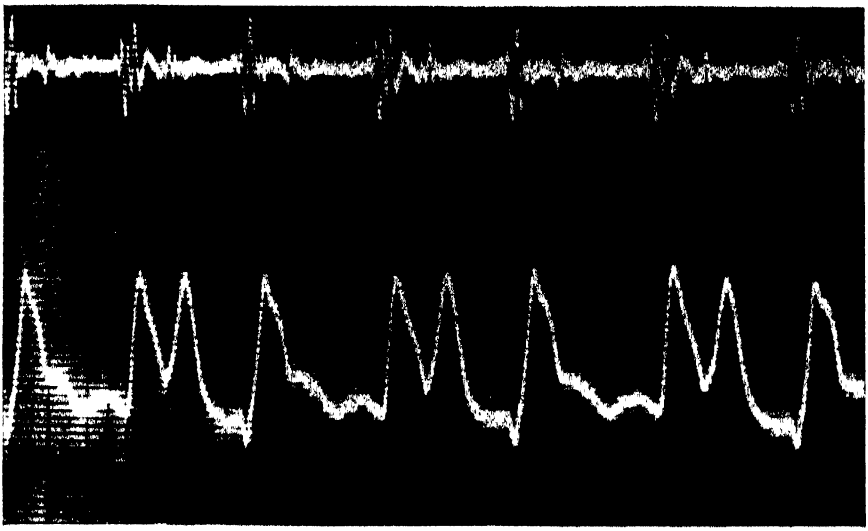


Fig. XXXIX.

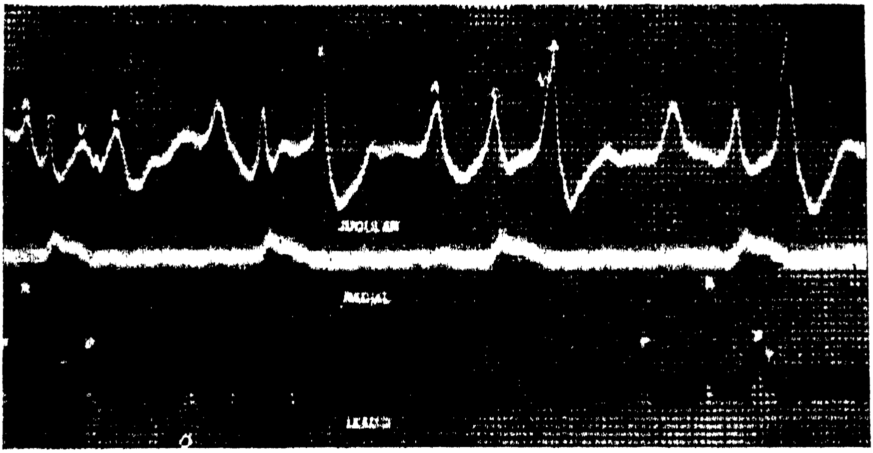


Fig. XL.

CHAPTER VII

MYOCARDITIS

By Alexander Lambert, M.D.

Definition, p. 319.
Etiology, p. 319.
Symptomatology, p. 322:—Acute myocarditis, p. 330; Chronic myocarditis, p. 332; Sinus arrhythmia, p. 338; Extrasystoles, p. 339; Paroxysmal tachycardia, p. 340; Auricular flutter, p. 341; Auricular fibrillation, p. 342; Heart block, p. 343; Stokes-Adams syndrome, p. 345; Pulsus alternans, p. 346; Ventricular fibrillation, p. 346.
Diagnosis, p. 347.
Complications and sequelae, p. 349.
Association with other diseases, p. 349:—Diphtheria, p. 349; Rheumatism, p. 350; Syphilis, p. 351; Influenza, p. 351; Neuroses, p. 351; Fatty heart, p. 355; Clinical variations, p. 356.
Treatment, p. 359;—Acute myocarditis, p. 359; Chronic myocarditis, p. 360.
Prognosis, p. 372.
Pathology, p. 375.

Definition.—Under the term myocarditis there is included today the acute myocarditis, which is an acute bacterial invasion of the myocardium, or an acute degeneration in consequence of infectious disease in other parts of the body; and also the chronic processes produced by the resulting scar tissue from the acute conditions, as well as the chronic connective tissue replacement hyperplasia produced by coronary arteriosclerosis, and by all other processes producing a degeneration of the cardiac muscle fiber or an increase of its connective tissue.

Etiology.—The acute infective myocarditis, in which the microörganisms actually invade the cardiac muscle, occurs infrequently as a diffuse process as a complication of the generalized infection in influenza, scarlatina, typhoid, diphtheria, gonorrhea, tonsilitis, or other streptococcus infections, or the staphylococcus infection of pyemia, or the myocardium may be invaded with the spirochetes of syphilis, producing an inflammation peculiar to this disease.

The more common form of infective myocarditis is, however, a form of suppurative inflammation, circumscribed and not diffuse, which results in minor abscesses; these occur in pyemia and other septic infections, and in the forms of ulcerative endocarditis as expressions of the general disease, spreading in multiple areas through the invaded cardiac muscle.

The diseases which cause a grave degeneration and acute intoxication of the cardiac muscle are diphtheria, typhoid fever, typhus, tuberculosis, pneumonia, and certain general septic processes from suppurative conditions or streptococcus infections, as infections in carious teeth or diseased tonsils, or general infections of the body. These all produce non-characteristic degenerative conditions of the muscle tissue, varying more in the degree of their intensity than in the different kind of degeneration produced. Rheumatism and syphilis, however, produce inflammation of the connective tissue framework itself, and rheumatism, with its characteristic Aschoff bodies, is the only involvement which can be said to produce a peculiarly characteristic pathologic change of the myocardium. The rheumatic infections tend to be confined to the left ventricle, and more in the region of the base and on the septum, than in the apex; syphilitic involvement in its early stages is a lymphatic and perivascular condition, producing a generalized specific increase of the connective tissue. The acute myocarditis is thus an accompaniment or, if one wishes so to consider it a complication, following infectious diseases in other portions of the body. Some degree of myocardial involvement may occur with any infection, and probably with all severe infections the myocardial involvement varies in its intensity. It may express itself only in slight variation from the normal in physical signs and symptoms, or goes on with such rapid intensity of involvement as to cause speedy death.

In the rheumatism of childhood particularly, rarely does the myocardium escape the rheumatic involvement. This myocardial involvement in young adults may be present without endocardial involvement, but, in all probability, judging from the resulting symptoms this endocardial involvement rarely takes place without some degree of myocardial inflammation accompanying it.

The syphilitic infections of the myocardium are much more common than is generally recognized, and occur as early secondary phenomena, although usually not recognized until in the tertiary stage.

The sources of chronic myocarditis still form debatable grounds, the main cause of disagreement seeming to be the inability of all investigators to agree on a common ground as a causation of muscular degeneration and connective tissue increase. There is no question that the acute myocarditis, whether caused by infections producing degeneration of the muscles or by multiple abscesses, leaves scattered scars throughout the myocardium or as in a recovery from intense degeneration of diphtheria, produces strands and connective tissue areas in the muscle.

These, however, are not the majority of cases, and actually form but a small number of the cases included today under chronic myocarditis. Rheumatism, however, with its Aschoff bodies is not like diphtheria, a morbid condition, definitely self-limited and definitely finished when its reactions have ceased. Rheumatism tends to recurrence, and tends constantly to fresh outbreaks. This in itself produces a recurrence of connective tissue growth and increase, with the resultant chronic type of inflammation. Syphilis, too, tends to chronicity in both the length of time in which its morbid processes are active, and in the type of inflammation that it produces. But although these two infections, rheumatism and syphilis, form the majority of the infections of the myocardium of childhood, youth and early adult life, and are common causes even on into middle age, there are, however, large numbers of patients showing no infective processes as a causation, and in the etiology of chronic myocarditis infections are not the dominating factor.

There are many causes in the body producing chronic degeneration, which appear after the years of youth and early life have passed, and after the power of recuperation, which youth and early life possess, have begun to wane. The habits of youth are kept up long after the vigor of the body justifies it; this produces overindulgence in food and drink, and with increasing responsibilities in many people, come increasing sedentary existence, and increasing worries, and nervous strain. These produce chronic intoxications and their resultant degenerations, both from excessive intake of bodily fuel, and from diminished output of detritus.

There are not infrequently conditions produced in the human organism which are best described as vicious circles. An excellent example of these is the condition produced by focal infections of the tonsils and teeth, or by pyorrhea. These little abscesses do not in themselves produce hypertension of the arteries, for infectious diseases are not the type that give increased tension in the blood vessels, but produce hypotension when they are the dominant morbid processes in the body. It is little realized that with each mouthful of food taken and swallowed when a patient is suffering from pyorrhea, or an apical abscess which connects with the mouth or infections in the crypts of the tonsils the contents of which are squeezed out in swallowing, each time the deglutition takes place there goes down with the food a mass of pyogenic organisms which before long pervert the normal digestive process into abnormal putrefactions, the abnormal products of which being absorbed, produce arterial hypertension, which in the end causes both hypertrophy of the myocardial muscle fibers and a connective tissue increase, and also a chronic intoxication and degeneration of the myocardial muscle.

We must consider the human organism as a whole, and not focus our attention too much on a single organ, if we would intelligently understand many of the degenerative processes which in the latter half of life are taking place, among these the chronic myocardial changes.

G. E. Farr in a recent article emphasizes the great influence of hypertension in the production of muscular hypertrophy with increase of connective tissue, and the resulting final breakdown of the heart from overwork. He also denies the influence of chronic infection as a predominant factor in this degeneration, although he realizes to the full the danger that the morbid changes of an acute infection, such as influenza, pneumonia, and any infectious disease, added to the chronic myocarditis, may bring to the myocardial muscle under the condition of its abnormal strain.

The cardionephritic condition, so-called, is another of these vicious circles, in which the kidneys are unable, for whatever reason, to excrete the decomposition products of the patient's existence, and there results the high tension and the chronic intoxication, often exhibited in the myocardium as excessive brown atrophy of the muscle, and the chronic muscular hypertrophy with increased connective tissue. These, and added to them the worries of existence, are among the causes which produce arterio-sclerosis. From whatever cause there be arterio-sclerosis, whether it be syphilitic or the general degenerative condition, if this vascular degeneration involves the coronary arteries, it causes a replacement hyperplasia of the connective tissue, and a degeneration and absorption of the muscle fiber.

We have not solved the equilibrium of the endocrine glands; we do not know the controlling mechanism between the thyroid and the pituitary and the adrenals. We see the breakdown of this equilibrium, whenever from excessive physical exertion or excessive worry, the resulting symptom complex of hyperthyroidism develops. We see the thyroid gland hypertrophy at times as a physiologic expression of over-action to meet the strain, when it would seem from excessive emotion the adrenals had been unable to perform their share of function, and we see the excessive thyroid over-production cause the breakdown of the normal equilibrium. We see worry, excitement and unhappiness, bring about an undue strain on the adrenals, and we see the expression of it in the hypertension produced by worry and the wear and tear of life, and these again produce the breakdown between the normal renal functions and the circulation. The inability to explain the chronic myocarditis may well be said to be due to the habit of the medical mind to separate the function of the heart from the function of the peripheral vessels, and to have separated the function of the circulatory system from its relationship to the function of the digestive tract, the apparatus in active function. It is unfortunately readily poisoned by diseases occurring in other parts of the body. It is subject to all the overstrain and chronic poisonings producing chronic degeneration of its muscular tissue, and is subject to incessant, never ceasing exertion, that goes on day and night as long as life lasts.

The diseases that affect the body come and go; they are acute, and they are recovered from, and the heart in the general recovery regains its health and vigor, or regains only part of its former normal vigorous condition of muscle and consequent reserve force; it retains within itself its scars and its permanent increase of connective tissue. In youth it possesses the unknown qualities of youthful recovery, and the algebraic sums of its injuries and recuperations do not seemingly permanently injure its extraordinary reserve power and the finely adjusted equilibrium of its reaction to its delicately balanced nervous mechanism. But after the years of youthful vigor are gone, the damages consequent to acute disease and the chronic poisoning of intoxications leave behind an accumulation of scars and injuries that break down its reserve force, and in the end first destroy its powers of ready response to all the demands which life makes upon it, and finally the morbid changes of some acute infection add the final straw to its overburden.

Starling has shown that the laws of the myocardial muscle are the same as those of skeletal muscles, and the laws of its physiologic dilatations and stretching are the same as those of other muscles, but it has a constant never-ceasing strain which the other muscles of the body do not undergo, and when from successive injuries of acute infections or the chronic intoxications, the degenerations are so great that it cannot overcome the increasing load necessary to open its valves, and drive out the blood, and empty its chambers, it begins to stretch permanently, and not contract normally, and the final breakdown comes when it cannot carry its overload. It still may answer the specific stimulations of drugs which increase the vigor of its contraction, or increase its momentary rest between beats, but successful management and prolongation of its existence comes from a protection against acute infections from without, and a due consideration of the human organism as a whole, and a relief from its poisonings and overstrain through a due consideration of the pathologic processes in the body external to the heart, and a breaking of many of the vicious circles in which the myocardium has become involved.

Symptomatology.—One cannot understand the evidence of myocardial disease, nor refer its early symptoms to their proper cause, if one studies it solely from the point of view of pathologic anatomy. Nor can we appreciate nor properly care for the milder degrees of morbid changes in the myocardium, if we wait until the symptoms of genuine heart failure develop. Heart failure does not occur until the myocardium is severely involved, and from many stages of lesser involvement it is possible for the cardiac muscle to recover completely, or to regain a vigorous condition.

The symptoms of the early stages of the acute or chronic myocarditis are the same as those we see and know in healthy human beings whose myocardium is out of condition or out of training. To understand properly the early stages of the milder forms of myocarditis, we must look to the explanations found in the physiology of the normal functions of the heart, and how they vary in individuals who have been trained, or who are untrained to undertake vigorous physical exertion.

F. A. Bainbridge has well summarized these in his monograph on the "Physiology of Muscular Exercise." When an individual begins to exercise there start from his higher nervous centers impulses which go to his skeletal muscles, and at the same time impulses to the respiratory center to increase its sensitiveness and to prepare it for the increased chemical changes produced by the increased necessity of the blood to carry oxygen to the lungs, skeletal muscles, and heart itself.

There are impulses sent simultaneously from the higher centers to the vagus center to lessen its tone, and also impulses sent which increase the tone of the accelerator nerves thereby producing an initial acceleration of the pulse rate. The nervous system thus prepares for a correlation of action between the respiration and circulation which prepares the way for the skeletal muscles to receive more blood, the heart to give and to receive more blood, and the lungs to furnish oxygen as ammunition to supply the tissue needs in action. The oxygen consumption of the body per minute during exercise varies almost directly with the amount of work performed, and there is an equally close relationship between the pulmonary ventilation and the oxygen consumption of the body. The greater pulmonary ventilation is gained by a stimulation of the respiratory center. How accurate is the adjustment of this center is seen by the fact that the reaction of the arterial blood varies very slightly, even during exercise, although there is both a rise in the tension of carbonic acid and a decrease in the bicarbonate of the plasma, due to the passage of lactic acid into the blood.

A man performing hard physical work may need and use eight or ten times as much oxygen as during rest, and the oxygen must be carried to the skeletal muscles and nervous system by an increased rate of circulation of the blood. This demands an increased output of the heart, which can be produced only by an increased number of heart beats per minute, or an increased output per beat from each cardiac systole. The increased blood supply to the heart is given by the contraction of the skeletal muscles, which squeeze the blood from their capillaries and veins into the larger veins, and thus into the right side of the heart, this return blood flow being also increased by the respiratory movements, particularly those of the diaphragm. Thus a larger cardiac output occurs through an increased venous inflow, and the diastolic filling of the heart dominates the increase of the circulation.

The output of the heart, per beat, depends on Starling's law of the heart, which is, that the force with which the heart muscle contracts during systole varies directly with the volume of the heart at the end of diastole; perfect adaptation would mean that with each diastolic increase of blood the heart should with each systole empty itself completely.

This the heart of the tortoise actually does, but the mammalian heart, according to Starling's experiments does not show this perfect adaptation. With the increased venous inflow the mammalian heart does not for a few beats equal by its output the increased inflow; for a few systolic contractions the heart is not entirely emptied, but each systole increases in force, so that in a few contractions the force of the systole is so increased that the heart has accommodated itself to the increased venous inflow. The heart also reacts in precisely the same way to a rise of arterial pressure, and after a few beats, becomes dilated to such an extent that it is able to maintain the same output against the increased pressure as that existing before the rise of pressure took place.

Bainbridge shows that there is no diastolic tone in the cardiac muscle, and the filling of the heart during diastole produces a dilatation of the heart which is normal, and this dilatation may go on under severe strain to the limits set for the filling by the heart of the pericardial sac.

Cardiac muscle, therefore, follows the same law as the skeletal muscles in that the force with which it contracts is directly proportionate to the length of the fibers just before they begin to contract. Every heart obeys this law, and the contractile power of the heart for any given diastolic volume varies with the nutritive condition of its muscular fibers, and a well nourished heart will contract more strongly and set free more energy than a badly nourished one. To obtain the same contractile force, therefore, a badly nourished heart must dilate more than a well-nourished one. Physiologically a diseased heart requires to dilate more than a healthy one, and it is evident from what has been said that the diastolic volume of the heart does not give any indication necessarily of its output per beat, because the unhealthy heart must dilate more to increase its output in response to the increased venous inflow. A thick walled ventricle, moreover, can increase its output with less dilatation than one whose walls are thin, whether it be required to overcome an increased flow from the veins, or an increased rise of arterial pressure; less dilatation will be required to obtain an equal force when the greater mass of muscle is present.

"The difference in behavior of the heart in different individuals as regards its output per beat can be readily accounted for along these lines. It is easy to understand that the powerful heart of the athlete while obeying the law of the heart, is able to respond to the moderate increase of venous inflow by much larger output per beat, whereas the smaller heart of the sedentary person, even if dilated to its physiological limit, can only moderately increase its output per beat. This is the true explanation of the difference in the so-called reserve power of the heart in different individuals. The calling up of the reserve is effective in accordance with the law of the heart, but the extent of the available reserve is determined by the contractile power of the heart, this depending partly upon its size, and partly upon its nutritive condition; since the latter are the variable factors, it is upon them that the varied response of the heart to exercise depends in different individuals."

An illnourished or diseased heart may dilate nearly to its physiologic limit with only a moderate rise in venous inflow, and yet obtain very little increase in output per beat; to obtain, therefore, a necessary increase in its minute volume under these circumstances such a heart must depend solely on the acceleration of the pulse, hence illnourished hearts must obtain increase in minute volume almost entirely by the acceleration of the pulse, while the healthy heart, with its great power, can double, or more than double its output before it dilates to its physiologic limit. The output of the healthy heart at rest is given as from 3 to 5 liters a minute, but it may reach even 20 liters or more during heavy work.

The rate at which the heart fills during diastole controls the effect of the increased pulse rate upon the output of the heart. If the venous inflow is small, with a uniform diastolic filling, the output per beat of the heart can be diminished, and yet the minute output per beat be scarcely influenced. If the heart fills rapidly early in diastole, even with a lessened output per beat, the acceleration of the pulse may increase proportionately the output per minute. As the output of the heart per minute is the product of its output per beat, the greater frequency of the pulse can compensate for the lessened contractile power of the heart muscle.

The persistent acceleration of the pulse during the period of exertion depends both on the continuous outflow of nervous influences from the cortex of the brain lessening the inhibition of the vagus, and also on those increasing the accelerator action; the diastolic dilatation of the heart also reflexly lessens the tone of the vagus. There is also a close correspondence between the intensity of the muscular work and the frequency of the pulse, and, as we have already mentioned, the nervous outflow to the skeletal muscles runs parallel to the impulse to the other nerve centers, and the increase of venous inflow to the heart is also in proportion to the muscular exertion being performed in the periphery. The maximum pulse rate during exercise has been found to be much the same in different individuals, that is about 160 per minute, and the maximum of the output of the heart per minute, which also varies in different subjects, has been found to depend upon its capacity to increase its output per beat, that is to say upon the contractile power of its fibers.

The efficiency of the heart diminishes if the acceleration of the pulse occurs without a corresponding increase in the output of the heart per minute, or if the heart dilates beyond its physiologic limit. Exertion taxes the resources of the circulation and the respiratory system equally with those of the muscles, and the circulation must maintain an adequate supply of oxygen to the heart, to the brain, and to the muscles. The adjustments in the circulatory system are more complex than those of the other two systems here mentioned, and the heart as a rule reaches the limits of its powers earlier than the skeletal muscles. The functional capacity of the heart, therefore, determines the limits of a man's powers or exertion.

There is a further nervous mechanism which increases the power of the heart and its effectiveness to obtain a larger cardiac output by increasing the blood supply to the muscles; that is, there is a constriction of the splanchnic vessels, and there is a dilatation of the vessels in the skeletal muscles and in the heart itself; the vascular contraction of the splanchnic area is due to nervous impulses from the cerebral cortex to the vasomotor center; whether or not there is a further chemical stimulation is unknown. It is believed that there is a chemical influence due to metabolic products produced in the muscles themselves which causes a further dilatation of the small arteries and capillaries in the muscles.

The rise of arterial pressure during exercise is the result of the increased output of the heart, with the constriction of the splanchnics and the dilatation of the vessels in the muscles and the skin.

The oxygen obtained from the increased supply of blood to the tissues permits the muscles to obtain and consume from 10 to 15 times as much oxygen as during rest, and the ability of the heart to increase its output is conditional upon an adequate supply of blood to its own muscles. It is stated that during severe exercise the heart may consume 100 cubic centimeters of oxygen per minute, and the flow through the coronary vessels may be 6 times greater than during rest. This increased blood supply is produced partly by the rise of the arterial pressure and partly by the dilatation of the coronary vessels.

Bainbridge emphasizes the fact that the blood supply to the heart is the weak link in the chain of circulatory adjustments during exercise, as a point is probably reached in most individuals at which the supply of oxygen to the heart falls short of its demands and the continued performance of heavy work becomes difficult or impossible.

There is the greatest difference in the effect on the heart whether with an adequate oxygen supply the cardiac nutrition remains normal, although the body may demand more than the heart can give, or with insufficient supply of oxygen to the heart an accumulation of metabolic products in the cardiac muscle fibers occurs, with the appearance of fatigue and an immediate diminution in both cardiac output and efficiency. This is the practical difference between the heart of youth and the heart of later life.

The effects of emotional stress on the increased power of muscular exertion is pertinent at this point, for the clinical evidence is too strong to deny that under emotional stimulation, whether it be of anger, fright, or other excitement, men carry out muscular efforts, of which, under normal conditions they would be incapable. This is produced mainly by the larger outflow and increased intensity probably of the nervous impulses from the higher centers, not only to the medullary centers but to the sympathetic system, which produces a greater ventilation of the lungs, a rise of arterial pressure, and an acceleration of the pulse, which permits sustained increase in the contractile power of the myocardium.

The question also arises here of the increased production of adrenalin under these circumstances, and although Bainbridge believes that its influence is comparatively small, even under emotional stress, the work of Cannon and Crile points distinctly in the opposite direction, and Cannon's work especially confirms the idea that the increase of adrenalin in the circulation is of great importance in relieving the fatigue of the muscle and in dilating the coronary vessels.

Bainbridge further discusses the difference between the trained and untrained man which practically is the clinical application of the physiologic laws of the heart. It is shown that regular and progressive exercise is the essential feature of training, and that the diet, if digested, is of secondary importance. The skeletal muscles consume for their energy the carbohydrates, and the heart can consume fats; the protein in the diet is not normally used as an energy producer for muscular exertion. Training develops the heart, and in a healthy man the cardiac corresponds with that of his muscular development. The increase of the contractile power of a healthy heart results in a larger output per beat, with a less frequent pulse rate than is present in an untrained man, even during periods of rest; the difference between a trained and untrained man, however, does not end with the difference in the contractile power of the heart alone, for while the pulse is less frequent in a trained man, and the arterial pressure usually lower, and the minute volume of the heart smaller, and the output per beat larger, there is also a greater coefficient of utilization and oxygen-carrying power of the blood.

There is therefore a more perfect equilibrium in the circulation of the blood as well as a greater ability to use the oxygen obtained. This is independent of the greater ease with which accustomed muscular effort is performed.

Bainbridge describes the characteristic features of the "second wind" familiar to all those who indulge in athletics, as due to "a simultaneous fall in the alveolar tension of the carbonic acid, and a decrease in the pulmonary ventilation, caused in all probability by the diminution in the H-ion concentration of the blood." This again is due to a greater mechanical efficiency of the body, and an improved blood supply to the muscles, and the exchange in the acid and basic radicals between the blood and the tissues. The increased size of the heart and the increased pulse rate in a healthy heart return rapidly to normal after the cessation of exertion. The return of the body to the resting state as regards its metabolism is more gradual, and the return of the pulse rate to normal is also gradual after severe exercise. The fatigue produced, and its cessation, is of two kinds, one a nervous phenomenon, in which there is no clear evidence to show that the products of muscular activity take any part in bringing about the sense of fatigue in the central nervous system. The fatigue felt in active muscles is different from that of the fatigue felt in the nervous system, and industrial fatigue is usually of a nervous type, for a trained muscle used to exertion will not show its fatigue as quickly as the nervous system. In the untrained individuals probably the nervous fatigue, as well as the earlier muscular fatigue, is in some measure due to a lack of oxygen to the brain and other tissues resultant from inability of the circulation to supply it; and the frequent occurrence of giddiness, faintness or nausea, indicates some degree of cerebral anemia, probably also due to an insufficient cerebral supply of oxygen. But in the trained individual at least, the usual sense of fatigue is probably due to the expenditure of nervous energy more than to a failure of the circulation or to the muscular decomposition products.

Besides the knowledge of the physiology of the cardiac function, there is necessary also for a proper understanding of myocardial function, a knowledge of the normal anatomy of the heart. Until recently the heart was looked upon as a single mass of myocardial muscle, which acted as a force pump, and was activated in its contractions, either by a spontaneous generation of muscle impulse within the heart itself, or else was a muscular pump and was accelerated and always controlled or started by nervous impulse from outside. The more our knowledge of cardiac anatomy and function has increased the less does one hear of myogenic or neurogenic theories of origin of the heart beat. Our increased knowledge of cardiac anatomy has clarified greatly our knowledge of the symptomatology of cardiac disease; we no longer, as formerly, regard the heart as simply a contracting mass of muscle; we realize that it possesses two systems; a contracting system of the main muscular portion, the healthy condition of which enables it to perform its function of equalizing and controlling the circulatory equilibrium of the body and disease of which may cause the break down of the circulation; and the conducting system in which each impulse to contract arises. This conducting system is a separate system within the myocardium, morbid changes in which produce separate symptoms from those of the diseases of the contracting system, and which acts as a controlling and regulating influence within the heart, thus controlling the contracting system itself.

The origin of the conducting system of the heart, which ends in its final development in the mammalian heart as the functional connecting link between auricle and ventricle, is commonly described as being embryologically the remains of the original cardiac tube, which curves on itself, and from the expansion of which, the auricles and ventricles are formed; this does not seem to be a sufficiently complete description. The final decision of its origin remains unsettled. Tandler holds that it is a development of a separate system showing as such even in embryos of 7–10 m.m. in length at a time when in the human embryo the continuous auriculo-ventricular muscles still enclose the two chambers and the auricular canal and its special tissues, but the interventricular septum is still unformed. It is thus a primitive connection of the two sections of the heart, or else it occurs secondarily after closure of the septum. Tandler holds that at no stage can the development of the bundle be followed towards the sinus. Against its secondary development Mall, Keith, Monckeberg and Aschoff have taken issue and hold it is a persistence of the connection between auricle and ventricle.

Ivy Mackenzie describes its development from the point of view of comparative anatomy, and shows how in the fish, this specialized tissue, in which the impulse starts is found at the junction of the sinus venosus and auricle and even at this stage the specialized muscle contains abundant nerve cells and fibers. Following its development through the reptilian stage to the mammalian heart he shows that as the sinus venosus becomes absorbed in the auricle this specialized tissue located in the auricular canal grows down into the ventricle as the ventricle develops upward and over it. This specialized tissue gradually becomes localized as a sinoauricular node and localized further as the auricular ventricular node in the septum of the auricles near the opening of the coronary sinus. The development of the auricular ventricular valves and the development of the interventricular septum cause this tissue to be partially absorbed in the first place and secondarily to be pushed into the muscular septum in a position of least strain.

The English view holds that the sinus and auriculoventricular nodes are remains of the specialized primitive tissue. But Monckeberg and others emphasize the typical position of the nodes in relation to the contracting valves of the primitive form of heart. The sinus-auricle and auricle ventricle, are intimately related to the neighboring valvular apparatus, the primitive function being related to or dependent on neighboring nervous elements. Koch holds that the sinus control has developed from dominating valvular control to stimulus initiation, i.e., cardiomotor function. The auricular node is normally of secondary importance in the heart beat which explains the anatomic and functional predominance of the sinus node.

The sinoauricular node is a small nodule of this specialized tissue containing nerve fibers and ganglion cells. It is situated at the base of the vena cava superior or in the taenia terminalis and seems to have no direct connection of specialized tissue with the auricular ventricular node.

This latter node or Tawara's node, as it is sometimes called from the name of its discoverer, has both an auricular and ventricular portion lying near the coronary sinus in the interauricular septum; it also possesses ganglion cells and nerve fibers and is prolonged as a definite bundle of special fibers passing forward and downward into the interventricular septum; in man it passes just below the membranous portion of this septum and separates into a right and a left bundle, the branch to the right ventricle passing downward to the papillary muscles, and spreads out over the ventricle ending in the Purkinje fibers which pass into and anastomose with the muscular fibers of the contracting system in the walls of the heart. The left bundle passes down the ventricular septum subendocardially and is thinner and flatter than the right and separates into anterior and posterior branches, and a small mesial branch passing down also to the papillary muscles and also ends in the Purkinje system. These bundle fibers are larger, longer and lighter colored than the ordinary muscular fibers; they contain more glycogen and transmit impulses less rapidly than the general muscles of the auricle and ventricle and much less rapidly than the terminal Purkinje fibers. The bundle is formed of longitudinous fibers with cross striations forming a syncytium, i.e., a solid connecting mesh work of fibers, not a parallel set of fibers separated from each other. This conducting system is separated from the rest of the heart in a connective tissue sheath, and Curran reports that there is demonstrable within this sheath a small amount of lubricating fluid.

Holmes states that the connective tissue everywhere forms a sheath not only for the whole tract of the bundle, but for each Purkinje fiber. Small nucleated nerves may be found in either branch of the bundle, and may be seen within the outer sheath of the branch between the separated Purkinje fibers. Occasionally small groups of ganglionic cells are found in the closest proximity to the Purkinje tissue. As the Purkinje fibers leave the endocardium they usually follow a small artery and become progressively smaller in all dimensions until they can scarcely be distinguished from ordinary myocardial fibers with which they are sometimes seen to be in direct continuity. A definite sheath of connective tissue and often small non-medullated nerves mark out the course of the Purkinje fibers. Wilson demonstrated in the bundle numerous ganglion cells and abundant nerve fibrils which may end in ganglion cells or in muscle plexus or pass through the bundle or form an intricate plexus around and in close relation to the muscle fibers.

Physiologically the sinoauricular node is the pacemaker of the heart, and the impulse starts at this point and goes to the auricles and to the auriculoventricular node, certain investigators pointing to the fact that it arrives at the Tawara node earlier than if it went through the general auricular muscle deducing therefrom that there is a direct nervous path between the nodes but no direct muscular one.

No special muscular tract has been demonstrated although Thorel claims to have discovered Purkinje fibers passing directly in the auricle between the two nodes; this has not been confirmed. Lewis gives the path of the auricular contraction wave as passing from the sinus node in all available directions, the wave as a whole spreading concentrically in the muscle of the right auricle passing up the superior vena cava against the blood stream, down the taenia terminalis to the inferior vena cava, from base to the tip of the right appendix, and across to the left auricle and appendix through the muscle bands which unite the two chambers. It spreads down the septum between the two auricles and eventually involves the whole musculature of the auricles and it reaches the specialized structures of the auricular ventricular node.

Any delay in the spread of the impulse from the auricle to the ventricle usually takes place in the auricular ventricular node. Lewis has shown that the rate of conduction of the A V node is the slowest of any of the cardiac muscle fibers and also that the length of its refractory period is the longest. To these factors he attributes the regular rhythmic blocking between auricle and ventricle in auricular flutter and fibrillation.

The blood supply of the neuromuscular contracting system is an important matter. Gross comes to the conclusion from a study of 100 hearts that a distinct and specific blood supply exists for both sinoauricular and auriculoventricular nodes, the main bundle and the first portion of the left limb and a large part of the right limb of the neuromuscular system, the remainder shows a supply which corresponds to the area of heart musculature on which it rests.

It is said that the sinoauricular node is supplied in 92 per cent. of the cases from the right coronary artery and in 8 per cent. from the left. The auricular ventricular node and the main bundle is supplied by a separate branch, the ramas septi fibrosi usually a branch of the right coronary. The right branch of the bundle is supplied by one of the earliest divisions of the ramus descendens sinister and in its final arborization anastomoses abundantly with branches from the right coronary artery coming through the muscular wall. The left branch of the bundle has no specific blood supply of its own but derives its nourishment on its main septal aspect from the anastomoses from the septal branches of both coronaries, the anterior limb of the main left branch receiving more blood from the left and the posterior limb from the right coronary. The final ramifying divisions of the left branch vary in their blood supply according to the situation on the musculature of the heart. The blood supply, therefore, varies in different hearts, but is, in certain main portions, sufficiently separate to escape degeneration from coronary thrombosis, which may injure and put out of function the surrounding contracting tissue and vice versa, the main mass of the contracting system may remain intact with good blood supply while thrombosis of the special artery supplying the neuromuscular tissue may destroy the function of the conducting system.

As we shall see under Pathology, Monckeberg already reports cases in which a differential degeneration of the two systems has been found.

ACUTE MYOCARDITIS.—The symptoms of acute myocarditis are usually masked as general symptoms accompanying the infectious disease from which the patient is suffering. They consist in increased rapidity of pulse rate as one would expect to find from the physiologic law of the heart and the extra demands required to keep up the circulation and to supply oxygen for the increased metabolism of the body under the general morbid conditions. The weakened myocardium may be unable to increase its cardiac output per beat, and if the diseased muscle fiber cannot stand this strain without going beyond its physiologic limitations of dilatation it responds with acceleraton of pulse beat. The severity of the myocardial involvement is shown by the degree of acceleration of the pulse rate and the success or failure to maintain the equilibrium of the general circulation. Infectious diseases usually produce a diminution in arterial blood-pressure, and the added advantage which exertion produces under normal conditions of a rise in arterial blood-pressure to increase the coronary circulation is absent, the myocardium is thus working with a diminished blood supply at an added disadvantage, both for its selfprotection and for fuel to enable it to perform the extra work required. The heart is working at a further disadvantage for with the patient in bed, there is no muscular exertion going on in the skeletal muscles to cause an increased venous inflow into the heart to help control the rate and to supply the necessary increase of blood to produce the increased output necessary for the circulatory equilibrium. In severe cases the slightest exertion brings on undue dyspnea and the respiratory rate is raised even during rest.

The nervous impulses to increase pulmonary ventilation and to increase the accelerator action of the heart are probably taking place but the circulatory response is working at a disadvantage from lack of proper blood supply. In moderately severe attacks of the infectious diseases these symptoms are slight during the course of the disease such as a short attack of influenza, or an attack of tonsilitis, or a moderate attack of typhoid or a mild attack of diphtheria, or any other infectious disease. The myocardial injury does not show itself until the patient is out of bed and in convalescence; it then is shown, however, by the inability to perform even moderate muscular exertion and breathlessness on going upstairs or in walking short distances is the most prominent symptom together with a premature sensation of undue and unaccustomed fatigue for the amount of muscular exertion made and it is noticeable that the pulse rate is disproportionately increased. In other words, the reserve of the heart is diminished because it cannot respond to slight needs by increased output per beat but must rely upon the disproportionate acceleration of the pulse.

The symptoms are similar as far as they are produced by the myocardial changes whether we are dealing with the infectious processes in which there is an actual microbian invasion of the heart muscle or whether it is simply a temporary degeneration varying greatly, however, in their intensity and in the clinical picture.

In the majority of instances the morbid changes are limited to their effects on the contracting system and cardiac arrhythmias appear only in the more severe cases, showing involvement of the conducting system. Diphtheria, however, is an exception, the degeneration produced in the contracting muscle is not infrequently accompanied by a degeneration of the bundle which may go on to complete heart block.

In very severe cases of infectious diseases with intense degeneration of the myocardium, seen probably most strikingly in diphtheria, the acute breakdown of the circulation and the signs of acute heart failure may develop suddenly and run its course in a few days. There may or may not be premonitory evidence of arrhythmia, there may be extrasystoles, or in some instances if an electrocardiogram be taken, there are also evidences of the prolongation of the P R interval showing the beginning blocking of the transmission of the impulse from auricle to ventricle. Then without further warning, great pallor may develop with apathy or sometimes a great restlessness and some dyspnea. Usually there is but slight increase of respiration, no dyspnea, and there is no cyanosis and but slight edema. There may be vomiting, sometimes severe cardiac pain, and there may be tenderness over the liver with an enlargement of that viscus. The rate of the heart in diphtheria may be rapid or slow, in other forms of acute myocarditis it is usually rapid, and the arrhythmia may increase with definite signs of a definite heart block. If the heart dilates there will be increased dullness over the precardial area and perhaps a systolic murmur due to the inability of the papillary muscles to contract properly and to prevent a lack of coaptation between the edges of the valves in either the tricuspid or mitral areas. Unless there is a marked nephritis present, there is but little albumin in the urine; patients may die in this condition in a few days; they may go on for several weeks and vary between slight improvement and periods of apathy and listlessness with few symptoms or vary in periods of restlessness and then finally die. They may go through these periods of varying intensity of the symptoms and slowly recover.

Those, however, who show a bradycardia with the sudden heart block recover less often than those who show simply a rapid pulse. In other words, where the conducting system is involved, as well as the contracting system of the heart, the condition is necessarily more dangerous to life. Monckeberg reports cases in which the bundle was involved to the exclusion of the contracting muscles. In pneumonia the arrhythmias not infrequently occur as extrasystoles, flutter, fibrillation, alternation and temporary arborization block have all been observed.

During the convalescence from typhoid and diphtheria the acute myocardial changes may cause sudden acute heart failure which after diphtheria may cause sudden death. Myocardial degeneration is also shown following diphtheria by instability of cardiac rhythm some patients at rest will show a normal number of pulse beats a minute, or even slightly lower, that is from 68 to 72 and yet on rising from a chair quickly and with no further exertion their pulse rate will increase suddenly to 120 or 130 a minute. This acceleration may follow the slightest exertion as walking quietly across the room or after similar moderate muscular exercise.

In this disease, however, there is a condition which resembles a paralysis of the vasomotor center and the accumulation of blood in the splanchnic areas simulating acute shock, producing the pallor already mentioned and adding to the disadvantage at which the damaged heart is working.

In all cases of endocarditis, whether of rheumatic or septic origin, the myocardium is involved to a greater or less extent, and the symptoms of accelerated pulse, dyspnea, and sometimes edema are the same as in acute myocarditis without the valve involvement. At times the valvular infection adds increased strain to the myocardium and dilatation of the cardiac chambers takes place with increased signs of edema, and increase of dyspnea and other symptoms. The acute inflammatory condition of its connective tissue element, as in rheumatism, may, through its inflammatory increase, cause pressure symptoms on the conducting system and the tendency of this inflammatory process to localize itself with the maximum of intensity in the left ventricle around the auricular ventricular opening causes an increased frequency of occurrence of disturbances in the bundle of His and often attacks of pain from pressure on the nerves.

Chronic Myocarditis.—The symptoms of chronic myocarditis differ from those of the acute myocardial degeneration, because of the fundamental differences of the pathologic processes in the muscle fibers. The acute processes are self-limited, lasting for a short time and tend to recovery in the majority of instances. The chronic changes beginning slowly tend to run along at a slow pace or remaining almost stationary develop the symptoms slowly and tend towards increased degeneration rather than towards recovery.

Dyspnea.—Those who permit themselves after youth has gone to lose their physical vigor, find at times suddenly when some slight increased exertion is to be made (and the same is true in those who habitually lead through force of circumstances a sedentary existence), that there is a sudden realization that they cannot go on with that exertion. There is an undue dyspnea produced, there is a sense, not of the old shortness of breath that they noticed in their youth but there is an unconscious sensation of beginning suffocation. It is more the difference between a desire for more breath and the conviction that one cannot obtain it. The reserve power of the heart is not noticeably diminished. It cannot respond by increased output per beat, and again responds as in acute conditions by increased number of beats per minute. This particularly is seen in the over-fat patients or in those in whom the arteriosclerotic processes have begun to limit the elasticity of the coronaries and these arteries can no longer supply the needed increase of blood to the heart.

In the early stages of chronic myocardial degeneration from whatever cause if moderate exercise is taken persistently, the cardiac musculature can be retrained back into vigor, not perhaps to the same vigor that it possessed in its youth but the early symptoms of dyspnea of increased pulse rate disproportionate to exertion, and the increased sense of fatigue following slight exertion and the inability to walk against a strong wind, to ascend stairs, do not mean that heart failure must necessarily follow as a logical sequence of these early symptoms. The myocardium can and will recuperate, provided proper treatment and proper regeneration of the heart muscle through continued exercise is undertaken.

That the early symptoms of myocardial diseases have not been generally recognized by the profession or the laity is due to the fact that the increase of pulse rate is produced unconsciously and that the shortness of breath is referred to the lungs and not to the heart; or referred to the general condition of adiposity that has been accumulating in the years of sedentary existence and the disproportionate fatigue following slight exertion is referred to the untrained skeletal muscles and due share is not accredited to the lack of condition in the myocardium.

Even in these early stages of the chronic degeneration slight acute infections add their quota of degeneration to the muscle fibers and the damage sustained under these circumstances lasts longer because recuperation from it takes place more slowly and the total sum of injury and recuperation left in the heart tends constantly towards the side of injury rather than to that of complete recuperation.

In men who have kept up their bodily vigor by exercise and have not permitted themselves to drop into an overfed sedentary condition, the passing attacks of acute disease may, it is true, leave their scars, but the balance towards recuperation enormously predominates over that of permanent injury.

During the periods, however, of acute diseases, the symptoms are the same as those of acute myocardial disease already described. When for against the idea that blood reaction is the determining factor in the control of breathing. Whatever the cause of the dyspnea may be found to be, certain it is that improvement in the vigor of circulation causes the dyspnea to cease and the exact relation between the inefficiency of the circulation and the accompanying dyspnea is not yet explained. Clinically the symptom of dyspnea is the commonest occurrence in cardiac inefficiency and runs parallel with the degree of inefficiency.

Edema.—The appearance of edema shows also the lack of power in the heart to keep up the circulatory equilibrium; edema is an excessive accumulation of lymph in the cells or intercellular spaces or in the serous cavities of the body and there is an accumulation of the fluid portions of the blood in the tissues.

The exact relation between the forces of hydrostatic pressure, of osmotic pressure, or diffusion or transpiration and of imbibition of water by colloids have all been investigated, and while their relationship may be calculated outside the body these relations are as yet too complicated to have been solved as they occur within the body. The influences of gravity are at times also noticeably marked and the edema in patients will vary markedly on the side of the body on which they are lying. At times the edema seems purely mechanical, at times it seems to depend as in the cardionephritic cases upon physicochemical reasons more than on mechanical. But in the early stages where it is present in the dependent portions of the body, as slightly pitting edema in the legs, and where it gradually increases and creeps up the legs, varying in intensity apparently by gravity, it is due probably more to the mechanical factors from the inefficiency of the circulatory equilibrium than any other condition, and in these cases it is especially the sign of the myocardial inefficiency.

Pain.—Pain as the symptom of both acute and chronic myocardial degeneration is a varying factor. It is frequently present during the acute disease and in convalescence following acute infections and is then more frequently described as a sensation of discomfort or of actual pain in the precordium and referred to the region of the apex beat on the chest wall. It may be simply a subjective symptom or it may go on to be accompanied by tenderness to touch and pressure in the skin and subcutaneous tissues over the precordium. It is frequently complained of by patients with slight degrees of myocardial disease following exertion with the dyspnea and marked increase of pulse rate and especially in those who suffer from chronic intoxications of alcoholism and tobacco. Any sensation of pain or discomfort in the precordium causes mental distress in the average person, and produces fear lest they may have some form of heart disease which will produce sudden death. The intensity of pain and its result therefore varies frequently in individuals and in the neurasthenic or the timid it has a corresponding intensity of effect in the symptoms of early cardiac disease. Pain in the myocardial diseases accompanying the chronic forms of endocarditis is not infrequently present and most often occurs in diseases of the aortic valve with stenosis and regurgitation. This location of endocardial infection is most frequent in syphilis and the syphilitic aortitis accompanying this form of endocarditis has probably a great deal to do with the frequency and intensity of the pain, because it is in this location, adjacent to the aortic valves, that the aortitis from this infection often produces the attacks of real angina pectoris. It also occurs with great frequency in mitral stenosis or in the double lesions of mitral incompetency and stenosis, which most frequently are the result of a chronic rheumatic infection with its increase of connective tissue of specially acute intensity, constantly contracting as all scar tissue does and producing an ever increasing pressure around the auricular ventricular opening where there is abundance of nerve fibers. Many nerves follow down the bundle of His in the interventricular septum and spread out with the Purkinje arborization. Clinically one observes the greatest amount of pain in those forms of coronary thrombosis which apparently occurs in the vessels supplying the septum. Cardiac pain is referred to the various areas supplied by the second, third and eighth cervical and the first eight dorsal nerves. The various ramifications and peculiarities of cardiac pain have all been described in detail and traced anatomically in the article on ANGINA PECTORIS and it is unnecessary to repeat them here. Pain is commonly ascribed to exhaustion of the cardiac muscle, but this is a conclusion which the clinical facts do not justify, as the most intense pain has not infrequently been found with normal myocardium and occurring after insufficient exertion to justify the opinion of muscular exhaustion of vigorous muscle. It is produced by the involvement in some way of nerve tissues and occurs most frequently and intensely in those forms of myocardial disease in which the connective tissue increase predominates or in which through arteriosclerosis there is a noticeable replacement hyperplasia of connective tissue. Rheumatism and syphilis are the infections which injure chiefly by connective tissue increase, and syphilis and other causes of arteriosclerosis produce the replacement hyperplasia. Pain is also present following the acute myocarditis but usually with rare exception in minor degree.

Nervous Symptoms.—The deficiency of blood supply to the brain produces various nervous symptoms as dizziness especially on change of posture, or sudden attacks of dizziness when walking which noticeably inspires the patient with a fear of falling. There is an exaggerated sense of exhaustion and fatigue even without exertion to account for it. Drowsiness or even stupor in severe conditions is not uncommon. Drowsiness after eating, which cannot be overcome, is frequently seen in elderly people. Headache is common. If there is much arteriosclerosis memory is impaired for recent events and prolonged mental effort is impossible. Hallucination of sight, hearing and smell are not uncommon. Figures of animals and persons passing through the room or standing by the bed are often vividly real and disturbing. Hallucinations of knocking or tappings or whistling or even heavy footsteps bring annoyance or fear to the patient. The hallucinations of smell are said always to be unpleasant. There is very rarely a sense of exhilaration or cheerfulness in a cardiac patient, especially of the chronic type. The sense of exhaustion brings depression, the realization of cardiac failure brings with it the sense of impending death and sleeplessness and bad dreams are common when they drop to sleep. Often the brooding fear that they may suddenly die each time they sleep greatly disturbs their rest. These patients feel that they are a burden and become suspicious and think the nurses or the family wish to be rid of them. Pain and discomfort add to their misery and irritability and edema and dyspnea further limit the little freedom of action left to them and actual retinal hemorrhages may diminish their eyesight. The congestion of the kidneys causes a high-colored scanty urine, and retention of metabolic decomposition causes often an active delirium with loss of orientation and unhappiness disassociating them from all causal relationship with their past, making them irritable, unreasonable and trying patients.

Chronic myocardial degeneration cannot be appreciated by a mere repetition of symptoms; it is an accompaniment, as we have said in its etiology, of any chronic deviations from the normal due to various breakdowns in the equilibrium of bodily function. It is caused by the chronic intoxications and acute diseases that affect the body and in its turn it influences and intensifies the severity of many of these morbid conditions.

Cardiac Irregularities.—One group of symptoms of myocardial disturbance require separate discussion; that is the irregularities of the heart beat.

Like all other symptoms produced by morbid conditions in the body the same symptoms or irregularities are produced by disturbances of functions as are produced by permanent organic change and damage. They may be generalized as exhibitions of increased irritability, as in extra systoles, or perversion of function, as fibrillation, or as inhibition and cessation of function in the diminishing ability to transmit impulses and the final permanently complete heart block.

These irregularities are produced through diseases in the conducting system, although the result is exhibited as an irregularity in the contracting system of the heart. The perfection of function, of course, is the regular equilibrium between the two systems and the resulting rhythmic contraction of the main mass of the myocardium. Excessive irritability of the conducting system may produce exhaustion in the contracting system as seen in paroxysmal tachycardia, where the main mass of muscle is made to contract with such undue rapidity that it cannot perform its function and may dilate and cease to contract altogether from exhaustion. While as a rule the cardiac irregularities can be divided into single occurrences it is not at all uncommon, however, to have two or three different forms of irregularity occur simultaneously in the same heart. It often requires great nicety of judgment to decide whether or not an acute arrhythmia is due to a disturbance from some acute or chronic intoxication rather than permanent myocardial change. As in all other myocardial disease the past and present history of the heart itself must be considered and the past and present algebraic sum of health and disease in the individual must be also taken into account in forming any judgment to obtain a decision based on the weight of probabilities.

SINUS ARRHYTHMIA.—Beginning with the sinoauricular node sinus arrhythmia is a variation in rhythm in which the stimulus is produced in the sinoauricular node and the heart responds regularly in slower or quicker succession under the variation of the stimulus. It is particularly noticeable in young people and is normal in children and young adults. The variation in the stimulus is due to the variability of nerve impulses in the vagus. The most common form is seen in the variation accompanying respiration and with each inspiration there is a quickening of the rate and with each expiration there is a lengthening of diastole and a consequent slowing in the rate.

These respiratory phases usually control the sinus arrhythmia, but it occurs independently without any relationship to respiration and may cause a general slowing of the heart even to such an extent as to cause syncope. There are no abnormal sounds accompanying it and the heart rate and pulse rate are synchronous and it disappears under the influence of exercise. It is a sign of health rather than of disease and it should be so regarded and as occurring most frequently in young persons with healthy muscles. Its variation with respiration is easily made out and it is characteristic.

EXTRASYSTOLES.—Extrasystoles are either premature beats developed in the conducting system of the myocardium of either auricle or ventricle or in the contracting system in either chamber or there may be genuine extra beats of ventricular origin appearing interspersed between normal beats of the ventricle. The interpolated beats or genuine extrasystoles are relatively rare, the premature beats either of auricular or ventricular origin are very common, or those even of the nodal tissue between the cardiac chambers are not uncommon. They occur at all ages, more frequently in men than in women, and are produced by many poisons and drugs such as nicotine, caffein, digitalis, atropin, adrenalin, muscarin and physostigmin. They are produced by indigestion and in some patients following the taking of certain definite foods, as in one patient of the writers, a physician, who noticed that after eating fresh pork all through his life, as a youth, as a young man and in old age it invariably was followed in a few hours by a disagreeable series of extrasystoles. The occurrence of these extrasystoles did not apparently follow any other food. They occur singly, or even in groups of two or three; they form the coupled beats or the triple beats following digitalis poisoning; in young people and in the healthy myocardium they are usually stopped by exercise, as probably they are produced under conditions which render areas in the muscle more irritable than the sinoauricular node and hence are more prone to break out as premature contractions in the lower rate than in an increased heart rate under exercise. Sometimes they are increased by exercise but this is usually in people over 50, that is in people who are most likely to have chronic myocardial changes; they also occur under vagal irritation as has been shown experimentally and as has been evidenced following emotional stress. Patients having undergone some severe fright or shock may have extrasystoles for several succeeding days.

Premature contractions are exceedingly common in neurotic individuals, even plunging the hands in cold water or other irritation of the skin may bring them out. They are very common in patients suffering from rheumatic endocarditis with disease of the mitral valve.

In listening to a heart which shows extrasystoles one is conscious that there is a regular rhythm in the heart interrupted by sudden breaking of the rhythm by a premature beat. If one has an unusual sense of time and rhythm, one may appreciate that the length of the pause following is of compensatory value; whether or not this is actually true must be made out by measuring the graphic records from either polygraph or electrocardiograph. The extrasystoles cannot always be differentiated from a slowly fibrillating heart but usually an experienced ear catches the regular rhythm of the heart interrupted by these premature beats. As has been shown in the electrocardiograph and polygraph records in the article on INSTRUMENTS OF PRECISION the auricular premature systoles are followed by uneven pauses while the ventricular extrasystoles are usually followed by a compensatory pause; that is the distance between the beat previous to the premature beat and the beat following it are equal to the distance between two regular beats of the cardiac rhythm.

Often the murmurs that are occurring in the heart are heard to occur with the extrasystoles or at times the lack of vigor of the extrasystoles is such that it does not produce a corresponding pulse wave at the wrist although it is appreciable over the heart as an extra set of sounds. These premature beats have at times a rhythm of their own and occur as in digitalis poisoning as one or two beats following each regular beat. Or regularly for long periods of time a heart will show a premature beat after every third beat and then after every seventh for example, or at some regular longer or shorter interval. At times the electrocardiogram shows that there is a regular alternation between the right and left ventricles as the place of origin of regularly occurring premature beats. There often seems to be due to unknown causes an underlying rhythm of their occurrence. Premature beats may occur without giving any sensation to the patient or they may cause conscious feelings of palpitation or thumping or as if the heart jumped or as they described it "flopped" or as if it turned over. A patient may be startled by the extra force of the beat following the compensatory pause or he may be simply conscious of a curious feeling of emptiness while extrasystoles are taking place. They may, however, cause the patient to start and even to cough at each occurrence of the premature beat. Many patients, however, are entirely unconscious of their occurrence. If they occur in paroxysms and they so occur frequently they may cause a feeling of distress and weakness and produce an active cardiac discomfort. Premature beats occur at any time in acute myocarditis either in the early period of morbid change or in convalescence. They occur also at any period of chronic myocardial degeneration.

PAROXYSMAL TACHYCARDIA.—Extrasystoles occurring singly as we have seen show increased irritability of the cardiac tissues. When this irritability becomes so intense from certain causes it may produce a prolonged and sustained condition of irritability in a focus extraneous to the sinus and dominate the rhythm of the heart. This produces a paroxysmal tachycardia arising in the irritable ectopic focus, which may have its origin either in the auricle or the junctional tissue or in the ventricle on either right or left side. It is seen more frequently in younger people, although it may occur at any age, and seems to occur more frequently in men than in women; it seems most frequent in younger adult life between 20 and 30, although relatively common between 30 and 50 years of age. While it may be an evidence of a functional poisoning in gastro-intestinal disturbances, it is also evident in hearts suffering from chronic myocardial degenerations, especially the atrophy and fibroid changes following a coronary sclerosis. It occurs in hearts suffering from chronic endocarditis and in hearts showing no valvular injury. Patients who are subject to this form of irregularity notice that it is brought about without any noticeable cause or whenever they are disturbed by flatulence or following some emotional excitement or undue physical exertion. Nearly all patients are conscious when the attack begins and ends and describe it as beginning with two or three extra thumps and ending as noticeably by a few short irregular beats of which they are conscious. It is almost always disturbing to their peace of mind and until they become used to it, it often causes a good deal of anxiety. In the severe cases it never fails to cause anxiety and with good reason.

The rate of the heart beat is usually between 150 to 200 and these paroxysms may last a few minutes or a few hours or for several days or there may be periods in which there is a continuous variation between normal rhythm and short paroxysms of this irregularity. Certain young patients in whom it seems to be a purely functional disorder may be very little disturbed by its occurrence, usually, however, there is a sense of palpitation and of bounding, accompanied by more or less sense of suffocation. There may be eructations of gas with nausea and vomiting. Hart reports one patient in whom an attack was invariably accompanied by watery diarrhea, and another patient by a frequency of micturition. There may be an acute precordial pain which may be of sufficient intensity to suggest an anginal attack with its radiation down the arms. Some patients complain of a numbness and tingling in their extremities. There may be with these paroxysms headache and dizziness and even in some instances it is accompanied with loss of consciousness of momentary or prolonged duration. If the tachycardia is prolonged there is a feeling of lassitude and weakness which may be accompanied by sweating and a feeling of coldness. In the very severe cases there occurs a dilatation of the heart with an acute distension of the liver and with sometimes intense abdominal pain. There may be a pulmonary edema and congestion accompanied with a cough and blood-streaked expectoration, the veins in the neck are swollen and engorged, and the patient is intensely cyanotic. In these cases there is evidence by percussion of enlarged cardiac dullness and the breakdown of the circulation is very evident by the edema in the extremities.

These paroxysmal attacks even in the severest cases may end as suddenly as they have begun and within a short time the heart will return to its normal beat, the symptoms subside and the patient recover his ordinary equilibrium of health. The pulmonary congestion and the edema of the extremities subside slower than the cyanosis and the sudden vanishing of the venous engorgement which was pronounced during the attack.

In patients suffering from chronic myocardial degeneration the occurrence of these attacks may be a very serious condition and the patient die in any one of the attacks.

The different types of tachycardia, whether it be auricular or nodal, or ventricular cannot be differentiated except by the electrocardiogram.

AURICULAR FLUTTER.—Auricular flutter is a condition in the auricles in which they beat between 200 and 300 times a minute in regular wave-like pulsations but all auricular pulsations are not transmitted to the ventricle, the ventricle answering only to every other, or every third or fourth beat of the auricle.

Lewis and his co-workers have shown that this irregularity is produced by the impulse travelling in a circular area like the circus movement of impulse in muscle.

Mayer found in studying the muscle of the jelly fish the impulses set in motion would travel around in a circle in an excised piece of muscle and found this also occurred in muscle cut from the turtle heart.

Mines and Gerry obtained similar effects in rings of muscles from a dog's ventricle.

Lewis explains the mechanism that in a ring of muscle, if an impulse starts from a given point, it can go upward and around on both sides of the circle, meeting at the opposite side of the ring. If, however, it is blocked because of the refractory state of the muscle on the left side of the ring for instance, and follows along up the right side, by the time the impulse comes around to the area at which it was blocked in the beginning, the muscle has recovered from its refractory state, and responds to the contraction, and the impulse follows then in a continuous circle in the direction it had started to the right.

Lewis has shown that the same circus movement of the impulse takes place in both auricular flutter and fibrillation, and instead of going through the regular channel, and repeating itself along these channels, the contractions of the auricle are so rapid that the impulse meets continuous obstruction in refractory and half-refractory condition of the muscles as this impulse wends its devious path, pursuing its endeavor from muscle fiber to muscle fiber, along cross links of the branching meshwork or along the ring of the muscle fibers as best suits the opportunity to find a path that permits its onward movement. In flutter the wave of contraction follows a constant anatomical path; in fibrillation this path varies from cycle to cycle. In flutter the refractory period of the muscles is longer than in fibrillation, and in flutter its refractory barriers of muscle are small; in fibrillation they are larger and deflect the waves along sinuous paths.

Lewis further describes one circle which the impulse takes in flutter of the auricle as following around the base of the large veins. The reason that every impulse of the auricle does not go through the auricular ventricular node to the ventricle is due to the fact that the refractory period of the node is much longer than the refractory period of either auricular or ventricular muscle; the impulse therefore arrives at the node before its muscle has recovered sufficiently to respond and transmit it. Lewis points out from his experiments that it is his belief that the quality of excitability of muscle is more associated with its conductivity than with its contractility.

Auricular flutter can occur at any time of life. Hart mentions the earliest subject of which he could find record as being 5 years old and that one of his own cases was 14 years old. It occurs, however, as a rule in patients in the latter half of life because the conditions which most frequently produce it are those of the defective forms of myocardial degeneration produced more by either scarring or the arteriosclerotic type of degeneration. Diphtheria and rheumatism are reported as causative agents, as well as syphilis. It accompanies the changes following chronic mitral disease, especially the dilatation of the auricle.

The fluttering condition of the auricle conveys no sound in auscultation and graphic records are necessary for its proof; it can be recognized clinically at times by the pulsations in the jugular vein in comparing them with the ventricular contractions as felt in the radial pulse.

Auricular Fibrillation.—In auricular fibrillation the auricular contraction is more rapid even than in flutter, but there is no regular contractile expulsion of the auricular tissue. The muscles contract in twitching masses of greater or smaller amounts.

The rate per minute often goes above 500 and the impulse through to the ventricle is blocked as in flutter at the auricular ventricular node, but goes through at very irregular intervals.

The auricular fibrillation is one of the commonest forms of heart irregularity, and produces the irregularly irregular pulsation so long familiar. It occurs most frequently in hearts that show a breakdown from chronic disease, either pure myocardial degeneration or rheumatic and syphilitic infections, especially following the endocardial lesions of the mitral valve which gives a stretching of the auricular tissue. It occurs at all ages, but usually in middle life; it is particularly the end result of rheumatic infections, as these occur most frequently in young adult life, and break finally in early middle life or the end of this period. Auricular fibrillation again shows as the evidence of breakdown of the chronic degenerative type of myocarditis not due to rheumatism and therefore occurs as the period of senescence appears.

Hart reports that he and Cohn have observed its occurrence in some 18 instances of lobar pneumonia. It follows attacks of influenza and often follows the chronic syphilitic infection and the degeneration from alcohol. Experimentally it has been produced by digitalis, nicotine and physostigmin.

The auricular fibrillation is easily recognized on auscultation in the majority of instances because there is no regular rhythm to the heart beat and there is no interruption of any rhythm. It is absolutely irregular. The proof positive in doubtful instances is the occurrence of the pulse deficit, that is, the difference between the apex beat and the radial pulse that is best taken by two observers, one counting the pulsations for a minute at the apex and the other at the radial simultaneously. If one must do it unaided then two successive minutes are practically of similar value when the pulse is taken for one minute at the apex and the next minute at the radial. This deficit is of double value; it shows the improvement under treatment as the fibrillation improves and it also is a good criterion of the value of the medication that may be given to improve the condition. Graphic records show conclusive evidence of the fibrillating auricle and in some doubtful cases are the final arbiter as to whether or not the condition still persists.

The relation between paroxysmal tachycardia of the auricular type and fibrillation and flutter is not yet apparent. There is a form of abnormal rhythm produced by excessive irritability occurring in the auricular ventricular node producing a tachycardia from this area. This is called the auricular ventricular, or atrio-ventricular rhythm; it is a genuine nodal rhythm. It has no particular clinical significance and shows itself in four types in the electrocardiogram; first, as given by Cohn, the auricles beat before the ventricles; second, the ventricular precedes the auricular activity, and, third, the onset of activity in both chambers is synchronous, or nearly so; in each of these three types the relation of auricular to ventricular contraction is sustained over long periods of time. The P R interval is shorter than normal, especially in the first type and in the second type the P wave is often inverted. In the third form, the P wave is buried in the R wave and the R wave exhibiting usually an increase in amplitude. In the fourth variety, the auricular P waves assume different positions from beat to beat, in respect to the ventricular R wave, and also vary from upright to inverted forms. This form of rhythm does not change the clinical picture of the chronic disease which it accompanies.

Heart Block.—The next group of cardiac rhythms is caused by a delay in the passing of the impulses or a blocking off more or less completely of these impulses. This can occur in the transmission of the impulse from the sinus to the auricle or the delay or block occur at the auricular ventricular node or in the bundle below or in any branch or area of arborization in either bundle to either ventricle.

This may occur as a purely functional condition at the sinus node, produced by vagal influences. It occurs anywhere in the bundle under the influence of infectious diseases such as pneumonia or diphtheria; it occurs under the functional disturbance produced by poisoning such as digitalis.

It occurs very frequently as a scarring from rheumatism or in the acute stage of the disease and, most frequently of all, it follows the injuries due to syphilis. It occurs sometimes as purely functional disease from poisonings of unknown origin in which no lesions can be found.

Sinoauricular block produces a slowness in the heart beat which clinically may be mistaken for a block lower towards the ventricle in the conducting system. It cannot be absolutely differentiated except by the electrocardiograph record.

The length of the pause is usually a little less than that existing between two beats of the cardiac rhythm and there is no activity of the heart during this period. If it is unduly prolonged, as it may sometimes be, syncope occurs and the condition may be mistaken for that of the Stokes-Adams syndrome which is caused by the disassociation between auricular and ventricular chambers. This condition is of vagal origin, as it is relieved by atropin. It may be that it is an exhibition of the normal vagal inhibition, as is seen in normal healthy individuals who all their lives have a bradycardia which may even be down in the fifties or upper forties as their normal heart beat, and this may occur as a familial peculiarity, the writer having seen it in three successive generations in one family.

Injuries to the bundle of His may occur in acute endocardial disease and a formation of an ulcer cause a penetration deep into the tissues with an acute inflammatory injury to the bundle, or the acute disease may cause degeneration sufficient to produce all degrees of blocking, not uncommon in diphtheria. Syphilitic lesions are probably the most common cause of the most irregular forms of arborization block in which the main branches of the bundle may remain intact, but interference with areas in either bundle affect the transmission of the impulse to a sufficient degree to change the normal electrocardiogram from either ventricle; or variations may be shown in graphic records, especially the electrocardiogram in the length of the P R interval, that is the time in which the conduction is delayed, producing a varying degree in different beats of partial block. When the block is complete and no impulses go through from auricle to ventricle, the ventricle then, after a pause, contracts with a rhythm of its own and there is the idioventricular rhythm initiated. If the impulse is delayed sufficiently from auricle to ventricle a single contraction of the ventricle may take place, or an escaped beat as it is called and then the regular rhythm of the ventricle go on. When heart block is present it permits of various associations of arrhythmia in the same heart. For instance, with complete block, and an idioventricular rhythm, there may be extrasystoles occurring either in the auricles or ventricles independently or there may be fibrillation of the auricle simultaneous with the complete block and the regular rhythm of the ventricle be uninfluenced by the fibrillation, or simultaneously there may be a rhythm of their own taking place. Heart block has been produced by stimulation of the vagus and as a result of asphyxia. Ivy Mackenzie mentions it as reported by Florence Buchanan as a physiologic condition in hibernation.

Various degrees of temporary or permanent block have been produced by injections of digitalis, adrenalin, aconite, muscarine and physostigmin. When any pulse rate is below 60 differentiation as to its cause should be made. On comparing the rate of cardiac contractions by auscultation with the pulse rate, it may be evident that many extrasystoles are occurring which do not send impulses to the wrist; it may be that there are occasional dropped beats produced by partial heart block. If the ventricular rate changes suddenly to half its normal amount a complete heart block is the usual explanation. If the change in the neighborhood of 30 or even as high as 45 be found in an examination of the heart in all probability it is due to a complete block, and this probability is the greater the slower the rate. At times one may hear the beat of the auricle during the silence of the ventricle. In the writer's personal experience this, however, although always mentioned, is not a common occurrence. This extra sound may occur so close to either first or second sound as to give the impression of reduplication of these sounds.

Hart mentions a rare heart murmur occurring in heart block during the period of ventricular silence due to an increase of blood flow from the auricle to the ventricle. This is first described by Mackenzie, but is of rare occurrence.

In the present fashion of giving massive doses of digitalis to correct fibrillations or even in infectious diseases such as pneumonia, it should never be forgotten that acute poisoning by digitalis may result and in which delayed conduction or even partial or complete heart block may result with increased difficulty in keeping up the circulatory equilibrium to be added to an already damaged heart. This is particularly true in rheumatism and in pneumonia, and the accumulative action of ordinary small doses of digitalis may in some individuals at the end of a pneumonia produce the same result; to anyone in hospital practice where the routine or frequent use of the electrocardiograph takes place this occurrence is not uncommon.

Although the circulation is often well kept up even with the idioventricular rhythm present there may be simultaneously present with the condition of heart block, a degeneration of the contracting muscles of the left ventricle and a heart may show the symptoms of myocardial degeneration under the ordinary influences of exercise or excitement. Usually when complete block is present the rhythm varies but little from moderate excitement or exertion.

STOKES–ADAMS SYNDROME.—The condition of Stokes-Adams syndrome which accompanies some cases of heart block should not be used as a synonymous term with it. This syndrome means the occurrence of loss of consciousness or convulsions accompanying sudden slowing of the pulse rate and sudden cessation of cardiac action in which the interval between beats is so prolonged that the patient suffers from cerebral anemia and loses consciousness followed with convulsions and sometimes with cyanosis. They may die in one of these attacks or the attacks may vary in intensity at different times. They may follow any slight or severe exertion or emotional excitement. Patients show distinctly individual variations in their greater degree of sensitiveness to these disturbing influences. These attacks occur more frequently during the period of partial block but increasing disassociation of the auricle and ventricles. When once the idioventricular rhythm is established the attacks of unconsciousness may cease altogether or may follow only excitement and undue exertion.

Pulsus Alternans.—Another form of cardiac irregularity is that of alternation in the size of the pulse as evidenced in the radial artery either to the finger or to the polygraph. The electrocardiograph shows this at times in the variation of height of the R wave but the graphic curves in the polygraph are the best means of studying its occurrence. This is described usually as due to varying strength in the contractile mass of the heart, a variability in the cardiac contractility. It occurs at all ages but usually during the years of senescence, as it is particularly common in the chronic myocardial degeneration rather than following acute infections. It may, however, show itself in the course of pneumonia, typhoid fever or acute rheumatic carditis; it occurs experimentally in aconite poisoning; it is reported by Hering in strychnine poisoning; it occurs in cases of chronic endocarditis with myocardial degeneration, and particularly in the non-infective degenerations of arteriosclerosis. It shows itself at times regularly in every other beat of the pulse; it is discovered sometimes in taking blood pressure where a variation of 10 millimeters of mercury may be observed alternating in the blood-pressure with every other beat of the pulse. It sometimes follows for several pulse beats after an extra systole; it is not uncommon as a concomitant occurrence with auricular flutter. In graphic tracings alternation may show itself in the apex beat or jugular tracings as well as in the radial, and in the jugular tracings there may be an alternation of either the A, C or V waves. In graphic records there may be a pseudo-alternans, due to respiratory influences. Hart mentions it as occurring especially frequently with a slow pulse, and a rapid respiration; the pulse rate is approximately double that of the respiration, the pulse waves coincident with inspiration are smaller than those that correspond to expiration. When the patient holds his breath, the amplitude of the pulse wave at once becomes uniform, which differentiates it from a true alternans. The cause of this condition, while usually given as varying contractility, is referred by others to variation in the conductivity and excitability of the muscles.

The recent work of Lewis shows that probably excitability of cardiac muscle is more connected with conductivity than with contractility, and alternation may be due to variation in the refractory conditions in the different diseased muscles, so that their excitability would vary as their refractory period may be prolonged. In aconite poisoning conductivity is interfered with as well as contractility, hence variations in the conduction in a diseased muscle may be the cause of the alternation as well as variations in contractility. The length of the refractory period may, however, account for both the variation in conduction and excitability and may account therefore for the diminution in both properties of the affected muscles.

Ventricular Fibrillation.—There is a form of cardiac rhythm, which is invariably fatal, that is, ventricular fibrillation. This has been produced experimentally in chloroform anesthesia and particularly in light chloroform anesthesia, in which adrenalin injection was made simultaneously. Sudden struggling or exertion would seem to add to this danger and it has also been produced by ligation of the coronary arteries. It seems to occur as the terminal rhythm in certain forms of myocardial degeneration, as in syphilitic myocarditis. It has been but little reported, as electrocardiograms have not been usually taken just previous to death. In one case reported by Robinson and Brideck there was a temporary recovery from this abnormality.

Diagnosis.—The diagnosis of myocarditis must often rest on the weight of probability as a complication of infectious disease. Often after a short attack of some infection the evident diminished tolerance to exercise indicates that the myocardium did not escape some morbid change. The diagnosis during the active period of the infection rests on the disproportionate acceleration of the pulse and the evidences of disturbance of the normal equilibrium of the circulation.

But the diagnosis of some degree of acute myocardial change must be accepted with all severe infections, and often mild infections, as being disproportionately intense in ratio to the apparent severity of the general infection and the myocardial damage occurs most often in hearts already damaged by chronic endocardial lesions and myocardial changes. The diagnosis of the recovery or continuation disease of the myocardium following acute infections must be made therefore by the ability of a heart to perform physical exertion without dyspnoea and without excessive increased rapidity of the pulse rate, and to maintain good circulatory equilibrium in the ordinary existence of the patient.

Chronic myocarditis is a more difficult diagnosis; the probability of its presence depends upon the history of the patient, whether or not he has had infectious diseases, which have left him less able to perform exertions which he formerly could do without consciousness of dyspnoea or fatigue. If these be present with a chronic endocardial murmur, the probability of a chronic myocardial damage is coexistent.

If in the middle-aged or young vigorous person there be a single murmur present, systolic usually, in the mitral area, or even diastolic over the aorta, and this patient can play tennis, and lead an active life with no evidences of cyanosis or undue consciousness of shortness of wind, the probability is that there is no serious myocardial change, and the diagnosis of myocarditis would not be justified. If, however, patients in the latter half of life, in whom there is an increased tension in the arteries, in whom there is an increased area of dullness over the pericardium, and in whom there may develop a gallop rhythm, the diagnosis of chronic myocarditis must be accepted. Even with increased tension, and chronic enlargement of the heart, the muscle may be still healthy and capable of carrying on increased function. If, however, there develop infections from long continued pyorrhea, from focal infections in the tonsils, or acute intercurrent diseases, such as pneumonia and influenza, the liability and probability of an acute myocardial degeneration must be realized, and the weight of probability is in favor of its presence. This usually before sixty tends to recuperate, but after sixty, intercurrent disease is more apt to cause permanent damage, and to increase or to begin the degeneration of the cardiac muscle with or without the increasing connective tissue.

The deductions to be drawn from a diagnostic point of view from the presence of cardiac arrhythmias and the discovery through instrumental examination of their presence, is of course of increasing value as the use of these instruments increases. In acute infectious diseases such as diphtheria, or during pneumonia, the sudden appearance of extra systoles increases the probability of the presence of acute myocardial degeneration. The appearance of delayed conduction, or partial heart block in diphtheria, or any acute disease, is the indication of the involvement of the conducting system in the acute degeneration. While the appearance of the rhythm in acute myocardial conditions indicates the presence of morbid conditions in the conducting system, it does not justify the diagnosis that these morbid conditions will go on into chronic degeneration or chronic myocardial changes of any kind. They may, or may not, increase the seriousness of the prognosis but that is another question. In acute conditions, however, they indicate the increased probability of myocardial involvement, and even in some instances, as in heart block in diphtheria, confirm the diagnosis. This statement should be qualified perhaps by the proviso, that if digitalis has been given in acute diseases, the arrhythmias may be produced by acute poisoning of this drug, and may not be due to morbid changes in the myocardium. Clinical observations seem to justify the opinion held by many observers that digitalis poisoning is more apt to occur. In acute condition of disease the presence of extra systoles, or paroxysmal tachycardia alone, are not sufficient to diagnosticate myocardial changes. Delayed conduction, and partial heart block, or paroxysmal tachycardia occurring in older people, with a history of disease, or in whom chronic endocarditis is present, do increase the probability of the presence of myocardial degeneration.

Flutter and fibrillation are probably always to be considered as indicating myocardial changes, even when no history of disease is present. No arrhythmias nor evidences furnished by instrumental examination can explain the presence of pain in the heart; they often are present with the symptom of pain, but do not account for its presence. Pain around the apex, and over the precordium points to acute infections or the chronic poisoning of tobacco or alcohol. Severe pain substernal or radiating to neck or arms indicates tobacco poisoning or aortitis, or a degeneration, acute or chronic, so severe as to involve the sensory motor reflex of the cardiac nerves.

The diagnosis of syphilitic disease is often one of pure exclusion, but if the patient has a history of that infection, if there is a sphilitic aortitis, or syphilitic involvement of the aortic valves, the probability of a myocardial involvement is so great that the diagnosis must be made on the weight of probability. With aortic valvular disease present between 25 and 40 years of life, and with an increasing cardiac insufficiency, which cannot be accounted for by acute intercurrent disease, the diagnosis of luetic infection of the myocardium must be accepted, even with a negative Wasserman reaction.

With all chronic kidney disease, there is a probability of chronic myocardial degeneration, and the two should not be separated, in the diagnosis. In the arterio-sclerotic degeneration of age, if an endocardial murmur develops, which though so often heard at the apex is usually due to lesion in the aortic valves, the increasing exhaustion due to exertion, the increasing dislike and inability to perform physical exertion, the decreasing standard of bodily functions, must be accepted as due to the increasing breakdown of the circulation and the diminishing power of the myocardium to keep up its former standard of circulatory equilibrium.

The unmistakable signs of chronic myocarditis are usually diagnostically slight, but edema, increased dyspnoea, with or without evidences of cardiac pain, with or without slight cyanosis, must be accepted as due to myocardial defects. When edema of the lungs is also present, even though slightly, and evidence of enlargement of the heart, the responsibility lies, not in making the diagnosis, but in failing to make it.

Complications and Sequelae.—Acute myocarditis is to be considered as an accompaniment or complication or symptom of general infectious diseases in the body, as an expression of the complication of some local or focal infection, and therefore does not possess complications in itself. When, however, an abscess of purulent myocarditis breaks into the pericardium the resulting purulent pericarditis is clearly a complication of the acute myocarditis. Chronic myocardial changes following the excessive scar tissue from acute degenerations or acute infections in the body are sequelae of these diseases. Chronic myocardial changes are sequelae from the chronic intoxication of poisoning by alcohol, or chronic tuberculosis, or carcinoma, and they are the results of the chronic intestinal intoxications and the breakdown of the bodily equilibrium, and metabolic changes of malnutrition. Acute myocarditis may well be said to be a complication of acute disease, when an acute degeneration is superimposed upon the chronic condition. It may be said perhaps that an acute breakdown of the circulation is a complication of an acute myocardial infection, added to the chronic myocardial degeneration; or it may be considered that the sequela of both acute and myocardial infections is a breakdown of the equilibrium of the circulation, and whatever consequences this may bring about, or may follow therefrom, may be said to be sequelae of the myocardial inefficiency.

Association with Other Diseases.—We have already pointed out that an acute myocarditis is associated with many infectious diseases, whether as an acute condition, or as an acute on top of a chronic condition. One cannot reiterate too frequently the probability of an acute myocardial condition being present in the body with an infectious disease nor can one emphasize too strongly the dangers to health and life that an acute myocardial degeneration of the muscle fibers bring during the course of a chronic non-infectious myocardial degeneration.

Diphtheria.—The variety and intensity of acute myocarditis differ with the general disease of which it is a complication, and the morbid process varies also whether the muscle or connective tissue bears the brunt of the morbid changes. The greater the intensity of involvement, the more prone is the conducting system of the heart to become involved. The pathologic degeneration of the muscle fibers themselves is practically the same, varying in intensity. They are most apt to be severely involved in diphtheria since in this disease from 20 to 30 per cent. of patients are said to show definite cardiac disturbances of sufficient gravity to affect the prognosis. With the great severity of muscle degeneration in this disease, there is also the degeneration of the conducting system. This also is extremely common in pneumonia and while the usual extra systoles are harmless when a casual occurrence in an otherwise healthy person, they become of very serious import when appearing suddenly in the acute infectious diseases, often showing the beginning development of a grave injury to the conducting system.

The degree of acceleration of the pulse rate varies greatly in the different infectious diseases. It is more apt to be slower in typhoid fever than in typhus or pneumonia, or puerperal sepsis, although in convalescence the reserve power of the myocardium does not seem to vary correspondingly.

In very severe cases of the muscular degeneration, particularly in diphtheria, the paralysis of the vasomotor control of the general circulation has become so intense that it too has masked the central failure of the myocardium, and the patient presents not the cyanotic dyspneic picture that one is accustomed to see in cardiac failure, but an intensely pale, apathetic, even somnolent patient, moving but little, with either rapid or slow pulse, dying quickly. Or again the picture is changed, and with the intense pallor and apathy, there is a stormy attack of intense vomiting, or the acute cardiac failure may be accompanied by a mild or severe cardiac pain, sometimes so intense that were it not in a child, but in an adult, would be called angina pectoris.

Rheumatism.—Rheumatism involves primarily the connective tissue, rather than the muscle. This, however, after a certain point is relative, because both tissues become involved, even in this disease. The endocardial involvement also varies the clinical picture, and the location of the inflammation in the septum increases the frequency of arrhythmias, due to bundle injuries. This also is true of syphilis, and here particularly the lack of characteristic symptoms has blinded our eyes both to the frequency of its occurrence, and often to the intensity of the involvement.

In acute rheumatic fever the myocarditis has also been hidden, because until recently attention has been focused on the murmurs produced by the endocarditis. The younger the patient, the more prone is both endocardium and myocardium, as well as pericardium to become involved, and in young adults the writer has seen several times pericarditis begin the picture of rheumatic fever in which the endocardial involvement developed several days later, or in other cases more rare, but of sufficient frequency to have left a very distinct picture in the writer's mind, are those patients who show no endocardial or pericardial involvement, but with their joint symptoms have marked acceleration of the pulse rate and cardiac distress disproportionate to the height of their temperature or the severity of their inflammatory symptoms. In some patients acute dilatation develops, but the usual picture, however, is that in a few days they recover from their acute articular involvement, the acute circulatory disturbance seems to subside, and the patient is considered recovered, and leaves the hospital, going back to physical work; the patient returns in a few days with a dilated heart, a high temperature, a dilated and painful liver, sometimes with congestion of the lungs, but with all the evidences of acute heart failure and broken down circulatory equilibrium. At no time in the disease does an endocarditis occur, because the acute murmurs heard during the period of dilatation of the heart subside and entirely disappear if the patient is fortunate enough to recover.

Not only with rheumatic endocarditis, but with all forms of endocarditis the acute myocardial degeneration takes place, the same as if the focus of infection were elsewhere than in the heart valve itself. A myocardial involvement may be in endocarditis more intense around the base of the affected valves, than when it is produced by some extracardial infection. The bundle of His lying so near the aortic and mitral valves is just so much more liable to become involved, and the peculiarity of the rheumatic inflammation to concentrate around the mitral opening increases the injury done in that area. The subacute progression of the disease or the cicatricial contraction of the healing scar tissue constantly narrows the mitral opening, accounting for the long observed fact that mitral stenosis was the one form of rheumatic lesions that was constantly progressive. It is often the persistence and progression of the myocardial lesion more than the endocardial which produces the stenosis.

Syphilis.—Syphilis deserves special mention as an infection producing cardiac damage, particularly myocardial injury. Syphilis in its early stages is a disease of the lymphatic system, and travels through the lymphatics until they empty into the thoracic duct, and then it becomes a generalized infection spreading through the venous blood to the heart and then through the arterial system. In involves early the vasae vasorum and their perivascular lymph spaces. The heart does not escape this early involvement, and although the morbid changes are relatively slow in their progression, they produce the active increase of the connective tissue in the myocardium and small gummata anywhere in the heart, especially in the intraventricular septum.

Many authors believe that acute cardiac involvement occurs only in the congential form of this disease. The work of Brooks, Warthin in this country and Grassman in Germany, have proved the incorrectness of their view, and have shown conclusively that cardiac and circulatory lesions in syphilis belong to the early secondary stages of the disease, as well as the later ones. Brooks in 50 syphilitics found the pericardium involved in 28, the myocardium in 47, and the coronary arteries in 35. This high percentage of cardiac involvement to the supposed general disease has only recently become appreciated. Clinically in the early stages of acute syphilitic involvement one cannot say that the symptoms differ from those of any other myocardial involvement. But the general symptoms of malaise, of fever, and of slight dyspnoea on exertion, of increase in pulse rate, even without fever, must awaken the realization that with the general infection having occurred, and with slight symptoms, possibly referable to the heart, the weight of probability of the myocardial involvement is very great indeed, and not as has previously been supposed, rare and a late chronic involvement.

Krehl emphasizes the fact that in his clinic fever in early syphilitic myocarditis is very common, usually of low grade intensity, but it may be of high degree, and of intermittent type.

Where syphilitic aortitis has occurred with or without involvement of the aortic valves the heart rarely escapes, especially if the aortic valves also are involved, with the probability of the involvement of the coronary arteries. But this type of myocarditis may well be considered as a clinical variety of chronic form.

Influenza.—Influenza, on the other hand, so dangerous in its myocardial damage to elderly people in the early stages of senescence, produces symptoms in which the nervous element of irritability, nervous exhaustion and excessive weakness, so predominate, that the symptoms of the acute myocardial degeneration are masked by the predominating picture of the nervous exhaustion and irritability.

Neuroses.—The late War brought out in strong contrast certain clinical types of myocardial disturbance which had been recognized individually in civil life, but the occurrence in large numbers emphasized it to such an extent that it was put under the special name of "effort syndrome."

Da Costa in the Civil War had spoken of the acute circulatory and cardiac breakdown in young soldiers overstrained by forced marching before they had become hardened to campaigning. Mackenzie had drawn attention in civil life to the fact that having an acute attack of grippe or tonsilitis, or some other apparently mild infection, young men as soon as they recovered might show disproportionate cardiac symptoms, such as fainting, and acute dilatation of the heart, following some athletic exertion, which previously had been done with no effort. This Mackenzie called the poisoned heart.

Besides in civil life there is a class of patients which all consultants see, whose nervous apprehension of cardiac disease, if intensified and applied in large numbers, would help to explain the puzzling clinical picture which those suffering from the effort syndrome produce. These patients are those of the apprehensive type, who after some slight infection find that they have shortness of breath and unaccustomed fatigue; they may or may not possess an extracardial systolic murmur in the second left space, but go to some physician who tells them that they have a murmur and that they must be careful, or the diagnosis is made of a "weak heart." In these patients such a diagnosis means heart disease, and heart disease means inevitably death at any moment, because in certain forms of heart disease sudden death does occur. The lay mind regards all heart diseases as associated with sudden death, being ignorant of the fact that the majority of persons having cardiac failure show the distressing and lingering type as their final picture. The fear of death, and the fear of sudden death, in the majority of humanity is a mental concept that produces ever present physical terror.

With the diagnosis of heart disease confirmed, and firmly established on a neurotic basis, with slight myocardial inefficiency from an infection, all symptoms immediately become greatly intensified. Hoffman in Germany, and Lewis in England report fully on this condition. The name of effort syndrome was given by Lewis to this condition, because in those patients who had no sign of structural disease it was found that the symptoms and the signs which appeared were those appearing in a healthy man who undertook strenuous exercise, it was also found in these patients that the degree of effort needed to call the symptoms forth was in inverse ratio to the malady and the signs and symptoms were the exaggerated physiological response to exercise: hence the term "effort syndrome." The sudden drafting of the man power of a whole nation involved in war tested the customary methods of military training, which had been usual for the small number necessary to train in peace time, and these methods broke down as applied to large numbers of men. Because when a whole nation is involved in training its youth, the saving of man power is a necessity, rather than the weeding out of the slightly unfit, and the point of view must change from that which endeavors to weed out as quickly as possible the slightly unfit from those who can stand unlimited strain without any consideration. The various bacterial vaccinations and inoculations necessary today in military life and the epidemic outbreaks of all sorts of infectious diseases in mild or grave degree and the bringing together of many physically untrained youths from sedentary existence, produce the combination of varying degrees of acute myocardial degenerations and many opportunities of over-exertion too early in convalescence among many patients. Added to this, in many instances, the sudden call from civil life to face a military existence in a great war in which the possibility and known probability of being killed was ever mentally present, the emotional and physical factors are combined in large numbers to bring about the clinical picture of the effort syndrome. As soon as the War ceased, the number of these patients immediately greatly diminished. The necessity for pushing convalescents into overstrain and overtraining, and into cardiac injury had ceased, and convalescence was allowed to go on normally and the patients recovered without undue physical strain on muscles showing acute morbid changes. This also reacted on those of slighter degrees of the apprehensive type, and no longer feeling that they were being pushed into certain death, as the strain on their hearts relaxed, they lost their apprehension, and quickly recovered. There remain therefore as an aftermath of the War only those inadequate personalities, who having passed through many physical examinations, have become thoroughly convinced because of the many conflicting diagnoses told them that they possess a deadly form of heart disease. Unable to shake off their ever present fear of sudden death, every physical sensation referable to their precordium, either slight pain on exertion, or quickening of their pulse rate under the slightest emotional or physical stimulation, increases the intensity of their anxiety neurosis. Wandering in the ever present disequilibrium of abject fear, they form the pitiful picture of the last remaining patients that show the effort syndrome.

The clinical picture of these patients is that they have breathlessness on exertion out of proportion to the exertion made, their respiration being as high as 40, 50 or 60 a minute on going up a short flight of stairs, or taking on the type of purely hysterical breathing respirations, run as high as 200 per minute.

Undue fatigue varies, of course, with the intensity of the symptoms, and in the mildest cases the patients suffer from fatigue on exercise similar to the average person out of training. The more severe the case, the more quickly is fatigue brought about by simple exercises.

Malaise and lassitude are specially common in these patients in the early morning and late afternoon. This fatigue may go on to exhaustion and actual collapse on exercise. Their weakness is further shown by the uncontrollable tremor of the hands, and of the legs which soon comes on during exertion. There is also a subjective sensation in these patients of a soreness from fatigue in the muscles, just as follows in healthy persons who, out of training, have done too severe exertion.

Pain in the precordium is very common in these patients in greater or less degree, varying from discomfort to an actual pain accompanied by tenderness in the skin, and sometimes to a stabbing pain, which they claim accompanies each beat of the heart. There is foundation in fact for this pain, but epidemics of all forms and intensity can rapidly take place in any ward among this group of patients, if too much attention is paid to it. It is usually the accompaniment in convalescence of morbid myocardial changes, due probably to the inflammatory exudate involving nerve ends.

Lewis brings out the point that the precordial tenderness is more frequently present in those in whom there is a past history of rheumatic fever, and these patients present a relative intolerance to exercise, when the pain may be severe, and may radiate down the left arm. The severer forms of cardiac pain occur in the older group, and the pain, if it be of serious import begins and is complained of as a substernal pain, the milder type, even that of going on to tenderness of the skin, is complained of as a precordial sensation. Palpitation is frequently complained of by these patients, and is due to a consciousness of their heart beat, and it may be due to extra systoles which disappear on exercise. Fainting is common either after exercising, or from some sudden fright, or may be due to lack of vasomotor tone producing anemia of the brain on standing. It frequently occurs after inoculation or vaccination, or the mere sight of blood may call forth an attack. Lewis points out that many attacks of fainting showed a lowering of the pulse rate, and the blood pressure accompanied with retching and vomiting which showed the attack was of vagal origin. Giddiness is not infrequently a symptom, usually appearing as a sensation of unsteadiness, without rotation, sometimes accompanied by blurring of vision, and the appearance of points of light. These patients frequently show excessive sweating, especially of the hands, and a steady trickle running from the axillae of these patients is very constant, even when stripped in a cool room. There is frequently a bluish red flush of the hands, extending up above the elbows, or there is a mottled appearance of the hands, and dermatographism is very common. Myotactic irritability of the muscles of the chest and upper arms and shoulders is also present to a marked degree. The rate of the heart in these patients averages above normal, usually averaging about 85 at rest; when up and about their pulse rate is even higher, averaging from 90 to 100; it may run continuously as high as 120 or 150 a minute.

In testing these patients, and comparing them with normal controls, Lewis found that the pulse rate varied in relation to the normal, as the dyspnoea of the normal varied with that of the patient. That is, given a certain amount of exercise, if it produced a violent dyspnoea in the patient, his pulse rate was correspondingly increased, no matter how long it took to bring about this condition, and in the healthy control the pulse rate would be correspondingly high if the exercise were carried out to produce an equal intensity of dyspnoea. The return, however, to normal is a much more valuable sign. With an increase in a healthy young man of 20 and 30 beats per minute the heart rate returns to normal in a minute or less, but the same amount of exercise would produce a rate of 120 or 130 per minute in these patients and the return to normal occur in a relatively longer time. In severe cases the pulse rate with slight exercise will go to 150 or 180 a minute, and take two minutes before coming back to normal. High pulse rates due to the stimulus of emotion occur very readily, especially in these patients, and single examinations are therefore of little value, and many of these patients use all sorts of tricks to bring about an increased rapidity of pulse rate by unseen exercise.

The blood pressure is within normal limits, and exercise produces the usual reaction, that is rising steeply in a half to one minute after the cessation of exercise, and then falling quickly. Here again if the respiratory reaction be used as a criterion of the amount of work done, the amount of rise in the blood pressure corresponds fairly well in these patients with the normal controls.

It is seen that the symptoms, therefore, among these patients are in the great majority those of excessive intolerance to moderate exertion but similar to those seen in normal individuals. They occur in patients chiefly because of the morbid changes produced in the myocardium after some infection, for over 80 per cent. of these patients gave a history of infection. The presence of fear of death, and the emotional instability in certain of these patients, produce the variation and domination of nervous influences, which render the clinical picture such a variable one. But even in these neurotic individuals, most of their reactions were those produced by exercise in normal and healthy people but disproportionately to the amount of effort necessary to bring them out.

Fatty Heart.—There is another form of acute myocarditis, which is known as a fatty heart. Pathologically this is given as of two forms, that of fatty degeneration of the muscle fibers themselves, and that of fatty infiltration between the fibers; clinically one cannot differentiate between the two pathologic conditions, and one must judge entirely on the physiologic basis of response to exertion as to the amount of lesion present. It does not necessarily follow acute infections, although there is no question that acute infections add their quota of injury and morbid change in those who have already fatty hearts. It is seen in patients who have in many instances been forced by circumstances to change an active life of youth to a sedentary life in early manhood and middle age, and who have retained their appetite and enjoyment of eating long after they had ceased to burn up the amount of fuel they consumed. This is seen especially in those who add the quota of beer and alcoholic beverages to a full amount of carbohydrates and proteids. Clinically, as one would expect, they show the dyspnoea on exertion and the increased pulse rate. If their heart becomes dilated from slight overstrain, as running after a train or pushing a disabled automobile, they will show an unusual amount of cyanosis with increase of dullness in the cardiac area. A fatty degeneration in the heart has in the writer's experience been present more in those who have taken large amounts of beer, and the increase of fluid with the carbohydrates, than in other forms of alcohol. In the office of coroner or medical examiner there are many instances of sudden death, in which the history is reported that the patient dropped dead in the street following a not excessive debauch. On post mortem examination the pathologic change in the cardiac muscle shows an extreme excess of fatty degeneration, whether it is the extra amount of alcohol taken that produces a muscle paralysis, or some sudden exertion under the stimulation of an excessive amount of alcohol, which produces the sudden death, it is a common occurrence in this type of cases. This condition is found most often in young prostitutes, who in complete physical idleness have consumed excessive amounts of alcohol.

Except in this type of fatty degeneration, which is of great pathologic excess, fatty heart has been given much more credit as a cause clinically of myocardial breakdown than has probably been justified. Pathologists have long looked askance on the relationship between heart failure and fatty degeneration, and without doubt clinically credit has been given to fatty degeneration, when it should have been given to an acute infectious myocardial degeneration added to a muscle grossly out of condition from excessive fatty deposits. Clinically, however, we must realize that in the overeating, self-indulgent fatty type of patient, his condition of excessive fat makes him correspondingly prone to serious myocardial degenerations if any infection add its quota of injury to the myocardial tissue, and the symptoms produced of dyspnoea, increased pulse rate, and if physical strain be put upon the muscle, dilatation and the consequent heart failure, are unusually liable to occur. Fatty degeneration of the conducting system as a cause of cardiac damage is mentioned by Monckeberg, but this type of patient does not show any greater tendency to cardiac arrhythmias than other patients suffering from ordinary myocarditis.

Clinical Variations.—Acute myocarditis in the majority of instances is an acute degenerative process as we have seen, but in scarlet fever, in streptococcus infections, or in pyemia there is a greater tendency than in the other diseases; for the myocardium, instead of being simply a seat of the degeneration of the muscles, is the seat of the actual spread and location of the infectious agents themselves, and there are under these circumstances purulent areas in the myocardium. These usually take on the form of tiny abscesses scattered through the tissue. The clinical picture does not vary except in the intensity of its symptoms, and in that they tend to be of the severe type. The abscess may break through the heart wall into the pericardium, producing a purulent pericarditis. This is also not uncommon in certain epidemics and types of influenzal pneumonia, in which the secondary infection following the influenza is the dominating type of infection, and in the years 1919 and 1920 in hospital service the infectious type of myocarditis and purulent pericarditis occurred with a frequency which had hitherto been unknown in the writer's experience.

The acute myocarditis is a process which in the majority of instances tends to recovery, but the morbid lesions may have been of such extent and intensity as to have caused an excessive destruction of cardiac muscle fibers. The process heals, but the healing is not with new muscle fiber, but with connective tissue scars; thus in severe cases though they may even recover from purulent myocardial infection, there is left an abnormal amount of connective tissue increase and scar tissue, or in rheumatism and syphilis this has begun as an interstitial type of inflammation and continues to progress with that type of tissue predominating. The muscle fibers themselves do not always fully recover their previous vigor, and may go into a condition in which the brown pigment normally present in a slight degree is observed in unusual amounts. This condition of brown atrophy also follows the chronic infections of tuberculosis or chronic intoxications of alcohol, or following the cachexias of anemia, or of carcinoma, produces a chronically degenerated form of myocardial tissue. This form of degeneration is also in excess in syphilitic hearts, in which the disease is of longer standing. It produces a tissue which cannot stand the strain of severe exertion, and also is a type which breaks down quickly under intense emotional anxiety and strain. It is noticeable clinically that small areas of pneumonic infections will produce death in patients in whom areas of chronic tuberculosis had brought about this chronically degenerated form of myocardial change. This type of degeneration stands the strain of operations or of acute infections very badly. The heart dilates and breaks down under any added burden in a few days, and the patient succumbs when he otherwise would have recovered had he possessed healthy myocardial tissue. This is seen often in women who have fibroid tumors of the uterus, and there has been an endeavor to connect the increase of brown atrophy in the heart with the presence of these tumors themselves. But both the French School under Vaquez and Krehl in Germany refuse to accept the causal relationship between these conditions. Clinically these patients show an inability to overcome slight infections, and show an undue proportion of cardiac weakness to any emotional or physical condition which brings strain upon the circulatory system. There may or may not be murmurs in the heart, and there may or may not be a cardiac enlargement on auscultation. There is, however, a noticeable embryonal type of rhythm to the heart sounds, the first and second sounds are of even value and evenly spaced; there is a tick tock character to these sounds, which is characteristic and of ominous import. These are the type of patients who, caught in a railway accident and seeing the terrible picture of the wounded, will in a few weeks break down completely, and sue for heart diseases brought on by shock, or undergoing some tremendous financial loss or other emotional strain, break down with a dilated heart.

The usual clinical evidence of an excessive connective tissue scarring in the heart after recovery from an acute disease is that, although the patient may apparently be healthy, and although still be in his youth, he has an abnormal shortness of "wind." There is a lack of normal response to physical effort producing an increased dyspnoea, which exercise or training, or which constant activity does not improve. The muscle tissue of the heart is permanently damaged and replaced by scar tissue, and it cannot respond normally to physical demands, the output per beat cannot increase as it should normally, even under training. The normal reserve is permanently diminished.

The clinical variations in the chronic forms of myocardial degeneration vary between the high tension groups without renal complications, the cardio-renal group, and the arteriosclerotic group. The clinical pictures of each vary proportionately to the number of attacks of acute infections that are added to increase the injury to the heart and the ability of the myocardial fibers to recuperate from each succeeding infection. The clinical picture is also very much varied, whether or not to the chronic condition there is added an endocarditis from any source, either the old chronic healed endocarditis of rheumatism or the added endocarditis in middle life produced by syphilis. At any time there may occur an acute septic or subacute streptococcus endocardial infection, which soon ends the scene. There are apparently differences of opinion as to the occurrence of chronic infections affecting the heart; syphilis and rheumatism are chronic infections both from the type of inflammation produced and the length of time the activity of the infections persist. There is no question that acute infections add damage to the chronic processes of cardiac degeneration. The rest of the discussion seems to rest upon whether an acute disease over long periods of time, such as infections from the tonsils or the teeth, should be considered as a chronic or acute or subacute infection. The discussion rests therefore upon whether the chronicity refers to type of inflammation produced or the length of time in which the morbid process is acting.

Syphilis and rheumatism may well be said to be chronic infections, both from length of time of their duration, and the type of their tissue change. But septic infections, whether produced in a short time, as in a single infection, or whether produced chronically over long periods, had best be considered as causing acute degeneration.

There is one clinical picture produced by the vicious circle between the focal infections of the mouth and the intestinal putrefactions produced thereby from the constant swallowing of pyogenic bacteria, and the resulting high tension in the circulation, producing a cardiac hypertrophy, both of muscular and connective tissue. If there is much systemic absorption from such a focal infection, there is added the continuous low grade poisoning produced by an acute infection acting on the muscle fiber through its toxins. This in the end produces an acute heart failure with acute dilatation and edema, and a very difficult type of circulatory disequilibrium to build up. There is a constant high tension and the constant source of damage to the muscular fibers.

Another clinical picture is that formed by the arterio-sclerotic type, in which as Jores has found there is an arterio-sclerosis of the minute arteries in the periphery of the circulation and in certain essential abdominal viscera. This in itself tends to produce a high tension from arterio-sclerosis, and there is again the disturbance of intestinal function, with a chronic enlargement of the heart, and chronic intoxication, in which there is a capillary degeneration and general absorption of the myocardial muscle fibers.

Another clinical picture is that of the cardio-nephritis in which there is glomerulo-nephritis, and the increased blood pressure from lack of kidney efficiency. The picture varies as to whether the kidney lesion dominates the scene or whether it stays somewhat in the background, and there is the high tension circulation with the hypertrophied heart struggling against a high diastolic pressure as well as high systolic pressure. After the heart has become hypertrophied and in which the equilibrium is in unstable balance, after it begins to show a necessity for careful observance of habits of life, and careful observance of a regime, then particularly is the time when acute disease, such as pneumonia, or influenza, or a severe tonsilitis causes a very disastrous breakdown in the circulation.

Janeway showed in his review of these patients that they broke down with cerebral hemorrhage, with uremia, or through heart failure. Any individual may show any varying combination of these factors, and as each factor predominates, so will each clinical picture vary.

In the nephritic type of patient there is apt to be a predominance of the attacks of dyspnoea, of the attack of varying uremia, and often with varying spasm in the smaller arteries in the nervous system, giving the appearance of cerebral hemorrhage. These clear up too quickly and completely to be due to complete break in the artery although a diseased artery may at any time close and cause a permanent blocking and even cerebral softening.

The arterio-sclerotic type also shows these same variations in arterial spasm, and shows more the irregular and unexpected symptoms in the clinical picture than does the high tension type, in which the degeneration of the arteries is not so prominent, nor the defect in the kidneys a treacherous and at times a dominating feature. This type shows also the greatest amount of cardiac pain and often has an unrecognized syphilitic basis. The coronary thromboses are also common in arteriosclerosis, and produce the striking picture of collapse with a sudden great fall of blood pressure, with leucocytosis and sometimes pericarditis. This common clinical picture is well described in Volume VI., page 36.

From the work of Gross on the circulation of the heart it is evident that after 60 years there is a progressive absorption of the small blood vessels of the right ventricle with an increase in those of the left side. With the added loss of resiliency in the larger vessels it is evident that there is a steadily increasing loss of power to furnish oxygen and nourishment to the right ventricle and a corresponding loss of reserve power. This increases the injury from acute infections. The heart apparently can withstand the strains of hypertension or of excessive exertion if its muscle fibers remain uninjured by infections or by certain chronic intoxications. But the constant recurrence of acute infections from which finally the myocardial muscle fibers can not recover is the dominating factor producing the heart failure in chronic myocardial conditions.

Treatment.—Acute Myocarditis.—Slight degrees of acute myocarditis noticeable only during convalescence from acute attacks of various infectious diseases, do not require treatment beyond an increased amount of rest and diminution of exercise; only if over-exertion has been indulged in and acute heart failure with dilatation occurs, would drug therapy be necessary. Rest in bed for a few days, and digitalis if the heart does not pull itself together quickly, will be required. The use of digitalis does not produce as satisfactory results as in the chronic myocardial conditions. In these cases which accompany the infectious diseases, it is a noticeable fact how often the use of digitalis is a failure. The acute heart failure of pneumonia is not helped by digitalis; in the early stages of heart failure of pneumonia sufficient digitalis to produce the increased vigor of systole seems of benefit, but when once the breakdown occurs, digitalis fails to act. We are dealing here with a type of morbid change which produces a degeneration of the muscle fiber, and apparently digitalis fails to act on a degenerating muscle. It is unfortunate that all our therapeutic criteria of drugs are based on the action of healthy cardiac tissues of animals, and we are forced to use them in conditions of unhealthy heart muscles in man, and we therefore have but clinical experience to guide us, and the experimental knowledge of what should happen were the muscle healthy.

In rheumatic carditis, where the inflammation involves chiefly the connective tissue and less the muscular fibers, digitalis seems to produce a more happy result, and especially is it of benefit, because there is the added muscular strain produced by the upset equilibrium due to valvular involvement.

The general care of the patients in their feeding, in the attention to their digestion and proper bowel action, is often of more benefit than the over-stimulation of their circulatory system. In the acute heart failure of these diseases, however, hypodermics of camphor and caffein are of assistance. The use in acute heart failure in infectious disease of adrenalin is often clinically of benefit; theoretically there is the discussion of whether or not adrenalin dilates the coronary arteries or contracts them, or whether or not it is advisable to raise the general blood pressure and increase the work against which the heart must act. In infectious diseases there is usually an abnormally low pressure, and the raising of the pressure with therapeutic doses of adrenalin does not produce a sufficiently marked increase in the pressure to be of any injury. Hypodermic injections intramuscularly of 5, 10 or 20 ♏ (0.3 to 1.3 c.c.) every hour for 4 or 5 hours will often rally a patient from collapse. There is the added debatable use of alcohol in the acute heart failure of acute myocarditis. In the early stages of the action of alcohol small doses increase the action of the heart and the volume of its output. When this stage is passed, it decreases the ability of the heart to perform its function by beginning paralysis of the muscles, it dilates the blood vessels and adds to the low tension, and also in many instances while it acts as a food, it diminishes the bactericidal power of the body. The algebraic sum of its value and of its injuries forms the debatable value of its usefulness.

In diphtheria we have the added factors of probable injury of the cardiac conducting system on which the action of digitalis is most noticeable. Digitalis in acute diphtheritic heart failure tends to increase the injured condition and the degree of heart block, and therefore is distinctly contraindicated.

Chronic Myocarditis.—In the chronic forms of myocarditis much may be done for the patients. In those forms of chronic replacement and scar tissue which are the remains of the healing of acute processes, we are dealing with a condition of the myocardium in which the muscles are fairly healthy and tend to recovery, but are inhibited from normal action by the increased amount of connective tissue. Those that show beginning heart failure and breakdown of cardiac efficiency are greatly benefited both by drug treatment and by the general training of the heart with muscular exercise, or the regulation of the tone and equilibrium of the circulation through baths.

Baths.—Considering baths in general it has been found that baths between 33° to 35° C. or 91.4° and 95° F. are in an indifferent zone, having little or no effect on the circulation of healthy individuals. Baths below that temperature are cool and cold baths, and baths above that temperature are warm or hot baths, depending upon the degree of temperature. Holst summarizes the effects of baths of varying temperature as follows: below the indifferent temperature zone they cause an increase in blood pressure, and a decrease in pulse rate; above the indifferent temperature zone, approximately up to 40° C. or 104° F., that is to say warm baths, cause first, a rise of blood pressure of short duration, then a lowering to the normal level, or even below it, and finally a fresh increase. The pulse rate is increased if the temperature is above 37° C. or 98.6° F., decreased if below; and third, baths above 40° C., hot baths, cause an increase in the blood pressure, in the pulse rate, and in the temperature of the body. The colder the bath, the greater the initial increase of blood pressure, the hotter the bath, the greater the final increase, and the nearer the bath to the indifferent zone, the less the effect.

The exact theoretical basis on which the equilibrium of the circulation in cardiac disease is improved by baths is still a matter of discussion and unproved opinion. In animals there appears to be a certain antagonism between vessels of the skin and internal organs, more especially of the splanchnic area, so that when the vessels of the skin contract the abdominal vessels and those of the lungs are prone to dilate, and vice versa, but in the human organism it is not proven that this takes place, and the circulation is more controlled by reflexes than it is by hydrodynamic processes.

The effect of a cool bath, according to Strasburger, gives exercise to the heart and lessens the work for it, but according to Muhler it increases the exercise, hence the labor of the heart.

Warm baths having a temperature between the indifferent zone and 39° C. produce a lowering of the blood pressure, while the systolic output of the heart and the pulse rate remain stationary, or are slightly increased. The work of the heart therefore becomes easier, but warm baths of this nature are not usually considered applicable to the treatment of cardiac disease, even though theoretically they would appear to be beneficial.

The addition of carbonic acid to the baths increases the reaction on the skin, and while the evidence shows that the most important effect is due to the temperature of the water, the gas content in the bath at the different temperatures acts as a kind of insulator, which helps the body to stand both cold and warm carbonic baths better than plain baths of the same temperature. There is also a sensory stimulation, partly mechanical by the pricking irritation of the carbonic acid bubbles on the skin, and partly chemical, irritating the peripheral nerve ends through absorbed salt and carbonic acid. A flushing of the skin is therefore produced due to changes in the vascular calibre and cardiac action. The increase of carbonic acid is also absorbed through the lungs, provoking an increased depth of respiration, hence increased flow of blood into the heart and increased ventilation in the lungs. Undue chilliness continued in the bath or after the bath, or a sense of fatigue produced by the bath, and listlessness, show that the bath has not been well borne, and contraindicate its continuance. Baths therefore in cardiac failure and as a means of improving the circulation are excellent in the milder degrees of cardiac failure, and especially as an additional adjunct to moderate regulated exercise. They are distinctly contraindicated in severe cases of cardiac failure; they are extremely useful among the type of indolent patients, and those who through a sedentary existence have acquired fat and begin to show a persistent, but mild degree of pain and breakdown of their circulatory equilibrium.

The advantages to be obtained are not only those of bathing, and increased circulatory action through baths, but also the advantage of a regulated life with regulated exercise under a regime in which the patient is cut off from the worries and fatigues of his daily routine existence. The advantages following are as much due to getting a man away from his daily routine and forcing him into a regulated amount of physical exertion and limited food intake, as in the baths themselves. It is useless to send the patient, whether or not he can afford it, to a bath cure, if his heart has refused to answer to all other methods of treatment. If there are any doubts about his standing the journey well, or any doubt, in fact, about his being injured by the fatigue of the journey, the journey and the bathing institution are distinctly contraindicated.

Psychological Influences.—Psychologically the effects of a regulated life, and any change from ordinary existence and often family worries, are of excellent effect on the patient, for the human race has great confidence in systems and regimes, and it improves the usual distressed and hopeless outlook that these cardiac patients as a rule possess. It improves the emotional equilibrium, and counteracts the incessant depression from autosuggestion on the part of the patient and from active suggestion on the part of friends who enjoy bringing in all the doleful incidents they have met in similar cases.

Exercises.—Regular exercise is of enormous value in all cardiac patients, but it must be regulated to the ability of the heart to perform its work. Many systems have been devised and described; Schott's system of bending each joint in the hand and wrist and arms, and raising the arms to the shoulder and up to the head, followed by bending of the body and the flexion and extension of each joint of the foot and leg and thigh, without resistance, and then followed by varying degrees of resistance, has proven of great value in the gradual gradations of exercise that a patient suffering from cardiac failure can undergo. It has the advantage that it does not need special apparatus, but the various apparatus of Zander doing things mechanically, leaving out the personal equation, and regulating the pressure accurately, has a great advantage in many instances; the apparatus, however, is enormously expensive, and but little used in this country.

Many patients improve materially under the gradation of the amount of walking on the level that they can do, and increase each day, particularly if there be various gradients, which they can take to test their cardiac vigor. This is based on the principle of Oertel's cure, in which he had the gradients of various hills mapped out which. the patients could take. This is particularly good in training the young, fat, overfed group. In treating the older patients under graduated exercises, the method recommended by Barringer produces excellent results. This method regulates the exercise through lifting dumb-bells and bars of varying weights a specified number of times; the continuation or the cessation being controlled by the reaction of the systolic blood pressure to the amount of exertion performed. Normally, as has been found, exertion produces an immediate rise in systolic blood pressure; if the exertion has been more severe than the heart can successfully manage, the rise in blood pressure is delayed. An immediate fall in blood pressure means failure of the heart to respond. The blood pressure is taken before exercise, and after exercise, as near the 30th, 60th and 90th seconds as possible. This method has been used both in the acute and chronic forms of myocardial degeneration by Barringer, Mann, St. Lawrence and others, and with benefit to the patients. This method has been criticized on the ground that the blood pressure reaction is not the most perfect means of measuring the cardiac reserve, and that there are other better means of judging it; even though true, this criticism would seem to be beside the point, the question being, is it of sufficient accuracy to be safely used in giving gradual exercise to patients during convalescence from acute diseases or beginning to show the early stages of cardiac failure? It has shown itself practically to be of sufficient accuracy to prevent accidents and injury to patients being exercised under its guidance, and has proved a very ready and sufficiently accurate criterion for practical use. Its advantages are that it is easily applied and used as a means of judging the extent to which exercise may be given to any individual patient. It is of sufficient accuracy to prevent harm, and under its guidance the patients show an increase in the amount of work necessary to produce the delayed action of the systolic blood pressure and improvement in their subjective and objective symptoms. The value of exercise to all patients when once the patient has reached the condition where this treatment may be applied is unquestionable; for beyond question the heart of the trained individual reacts more easily to any given exertion than the untrained, and the varying degrees of injury from acute disease or chronic degeneration produce in the heart the diminution to exercise tolerance that the myocardium of the untrained individual shows.

Each function in the body improves by its exercise, and a heart is no exception to this rule. The only question that arises is when is a patient sufficiently well enough to have exercise applied as a therapeutic measure. No one would endeavor to take a patient out of bed and exercise him as long as any rise in temperature existed, nor would one attempt to, if the patient showed much dyspnoea at rest or was not sufficiently convalescent to be up and about; but the fact that a patient shows beginning heart failure, shows cardiac degeneration or endocardial involvement, should not relegate him to the invalid class, which in recent years has too frequently been done. Many a damaged heart can go on and be trained to perform its function sufficiently to enable its owner to lead a comfortably active life, and certainly not that of an invalid; and many an individual keeps himself in good health, and increases the number of his years of life by self-restraint in eating and drinking and smoking, with regular indulgence in as vigorous exercise as his heart permits; that is, he is governed by the amount of dyspnoea on exertion, and the amount of fatigue following exercise, and experience gives him the wisdom to vary the amount of exertion from day to day.

Teeth and Tonsils.—The various types of chronic myocarditis often require more treatment for the general condition of the patient outside of the heart than treatment focused on the heart itself. Patients showing focal infections in the mouth, with the constant swallowing of pyogenic bacteria, will show great improvement as soon as the pyorrhea is cleaned up, the carious teeth cared for, or the apical abscesses removed or properly drained, and the tonsils extirpated if they are the seat of focal infections. This in itself produces in a surprisingly short time improvement in the subjective feeling of the patient and in the improved equilibrium of his circulation.

Gastrointestinal Tract.—Many of the high tensioned patients need special care of their intestinal fermentation, and this may be obtained by intestinal disinfectants, such as salol and castor oil in five grain and five minim doses respectively, four times a day, or the continuous taking of the lactic acid milk with or without the addition of a teaspoonful of milk sugar with each glass of milk. These patients also show a great improvement if a series of colonic irrigations are thoroughly applied. The fermentation in the colon may be so firmly established that the colonic irrigations may have to be continued for a considerable period. Some patients show the carbohydrate type of fermentations, and others the type of the putrefaction of their proteids. Their diets must be regulated accordingly, but many patients that would seem to require special diet do better under a general diet, but moderate in the amount of food taken. These patients if they are tending to lay on increased fat also should be forced to go through for a year or more the disagreeable regime of cutting down the actual amount of food taken and having to resist their tendency to eat, although they are more or less hungry continuously. This applies specially to the patients showing fatty type of cardiac injury. Worry and strain with the intestinal intoxication bring about the forms of arteriosclerotic degeneration, and these patients also must be regulated in their life. Often the addition of small doses of iodide of potassium is a valuable adjunct to assist their improvement. In the non-syphilitic cases it is as effective as in those suffering from this disease. Its action in the body under the alterative class in which it has been placed is distinctly one of stimulating the action of the thyroid gland, and many of these patients show the dry skin, the easily chipping nails, and the dry hair of patients suffering from a hypothyroid condition. Stimulating the patient's own thyroid acts often better than giving him thyroid tissue itself.

Diet.—In treating patients of a cardio-nephritic type one has to weigh the evidence as to whether the nephritis or the cardiac insufficiency is the predominating factor. The functional kidney tests give the best criteria of how much the kidney is involved, and added to this the height of the diastolic pressure is of great value. Often here the choice must rest between the dry diet of limited amount, or limited fluids, where the heart seems to be the dominating cause, and of increase of fluids and a more careful regulation of the diet, where the damaged kidney predominates.

Balfour some years ago recommended a very careful restriction of the diet, with only a glass of fluid with each meal, or a glass of fluid half an hour before the meal, with the weak tea or coffee taken with one meal, and this especially in those cases in which there was slight edema of cardiac origin beginning to show, and in what he described as the senile heart. If, on the other hand, there is marked cardiac breakdown with great edema and marked dyspnoea and distress, the Karrel cure of limited amounts of milk is of great value. The usual regime under these circumstances is given as follows: 200 c.c. or 6 oz. of milk is given at 8 A.M., at noon, at 4 P.M., and 8 P.M. for five to seven days. For the following two to six days bread, two eggs, minced meat and vegetables are given, with 800 c.c. of milk, and from the seventh day onward, the patient is put on his ordinary full diet. With this goes limitation of other fluid and the patient must be entirely limited to this. Sometimes during the last three days of a seven day cure, a full quart of milk, 1000 c.c., may be given. In some recommendations for the Karrel cure skimmed milk is given, and it is the most effective as a diuretic for rapid reduction. Other physicians give the full milk instead of skimming it. Often when patients complain bitterly of hunger during this Karrel cure one or two small crackers with each glass of milk does not detract from the efficiency of the treatment and eases the pangs of hunger.

In recent years there has been much discussion as to the necessity of a salt-free diet in edema. In some patients the amount of edema varies with the supply of salt; in others it does not, and in some cases of kidney involvement, there is evidence of salt retention, in others the giving or withholding of salt does not make any difference, and there is no salt retention. Paltow has shown that food is digested well often in the proportion in which it tastes well, and in many of these chronic invalids, the improvement of their digestion and general condition is of great importance, and the question of withholding their salt and giving them insipid flat tasting food is a matter of a good deal more moment than is usually appreciated. Unless in any given case it has been proven that the withholding of salt is necessary and adds distinctly to the improvement of the patient, it is not worth while to add to the patient's discomfort by withholding the ordinary amount of salt with which his food is cooked.

Tobacco.—The question of the use of tobacco is certain to arise in cardiac patients. Beyond question tobacco in certain individuals produces extrasystoles, which cease when the tobacco is stopped. It also increases the pulse rate and increases the systoles proportionately. It long has been observed to shorten the "wind" even in the young. In the arterio-sclerotic type of heart it increases the amount of pain and increases the frequency of the pain. In those patients suffering from angina pectoris this is especially true, and tobacco increases the liability of the attacks and the intensity of the attacks. Under the article on ANGINA PECTORIS we have gone thoroughly into this question. The effects of tobacco, however, vary in the individual, and in some patients, even in those suffering from moderate degrees of myocardial disturbance, a moderate amount of tobacco does not seem to harm certain individuals and patients will often limit themselves in the amount of tobacco used, because of the realization that in them, at least, it does injury. The stopping of smoking to most men is more of a psychologic annoyance than a physical discomfort, and when once accomplished is soon forgotten.

Alcohol.—As to the mooted question of the use of alcohol—in young patients, in those who are prone to overeat, and in the majority of individuals, alcohol does more harm than good. In elderly patients, suffering from brown atrophy and the chronic forms of degeneration, alcohol in some instances may improve their digestions, and in moderate amounts taken with their meals it is of benefit to certain of these individuals.

Climate.—Cardiac patients do not bear well extremes of climate, and a cooler climate from the excess of summer, and a warmer climate from the excess of winter adds to the prolongation of the existence of the chronic cardiac. In general cardiac patients are more stimulated and do better in the hills, not above 4,000 feet, than they do at the sea shore. High altitudes, because of the effect on blood pressure and the increase of dyspnoea on exertion, are to be avoided. It has been reported that high altitudes reduce blood pressure in cardiacs. The sudden reduction of blood pressure may be the cause of the occasional collapse of some of these patients in railroad trains going across high altitudes. In certain patients suffering from high tension with attacks of angina, high altitudes have not seemed to cause them any injury, but rather to make them feel improved, provided, however, that they do not take exercise, but exertion at high altitude brought on more quickly attacks of pain than at low levels.

Drugs.—*Digitalis.*—The drug treatment of heart failure has become more and more reduced to the value and the intelligent use of digitalis. Eggleston in his study of the digitalis group of drugs has found that the different preparations and different forms of digitalis are absorbed with varying rapidity. Strophanthus, convallaria, squills, apocynum, and others of the group are poorly absorbed. Strophanthus is 100 times as active as digitalis, and is usually given in the same doses, but its varying effect is due to its varying degrees of absorption. White, in studying squills and its effect as compared with digitalis, has found that it does produce a digitalis-like effect, provided that it be given in doses of from 2 to 5 drams, instead of 15 minims as recommended in the United States Pharmacopoeia. Clinically it also may produce nausea and disturbance of the digestion before any digitalis action is produced. The actions of digitalis and digitoxin persist longer than those of other members of the group, the effects lasting in some cases even two or three weeks after administration has ceased. Strophanthus on the other hand, ceases completely in 48 hours after the cessation of its administration. Crystalline digitoxin as given in Nativelle's crystalline digitaline represents all the active constituents of digitalis, and is rapidly absorbed, and more uniformly than digitalis. In doses of a quarter of a milligram, 1/250 of a grain, it is an extremely active preparation, and from the rapidity of its absorption and its activity requires care and skill in its administration. Digipuratum is probably the most satisfactory of the many proprietary forms of digitalis now on the market, and it has the advantage also of being useful in its ampules for intramuscular injections. For administration by mouth, the average tincture of digitalis produces good *and fairly uniform results.* For very rapid absorption, the intravenous *method is the quickest.* Eggleston states that the fluid extract of dig*italis and the tincture of strophanthus may be injected intramuscularly, and the tincture of digitalis may be injected intravenously if well diluted with distilled water.*

The most active intravenous preparations are the ouabain (crystalline strophanthin-G of Thoms) or the amorphous strophanthin. These intravenous preparations should be injected in dilute form, ouabain not in greater concentration than 1 to 4,000, and strophanthin not in greater than 1 to 1,000. The intravenous injections of these drugs are not without danger of sudden death, and they should be used only in emergency, and the injections given slowly in the above diluted forms.

Recently the bio-assay of digitalis preparations has been used as a standard. Unfortunately many standards and different animals have been used, and it is not possible to compare the different standards one with the other. It does not necessarily mean that the dose as given according to any standard is expressed as the relation of the dose to be given to man.

The usual method to secure the full effect of digitalis as soon as possible is by giving small or large doses, according to the degree of heart failure, and the rapidity with which effects are desired. Eggleston's description of the small dose method is 0.12 to 0.25 gm., two to four grains of the powdered leaves, or 1.25 to 2.5 c.c., 20 to 40 minims of the tincture, should be given 4 times in the twenty-four hours, and continued until digitalization occurs. With good preparations of digitalis this takes from 4 to 6 days; with weak or poorly absorbed preparations, from a week to ten days. With the large dose method, during the first 24 hours a dose of 0.4 gm., 6 or 7 grains, of the powdered leaves, of 4 c.c., a dram of the tincture, are to be given every 6 hours, for the first 24 hours. On the second day the dose is cut in half and the interval shortened to four hours between doses, by giving only 4 of the doses in the day and cutting the night dose. This dose of 0.2 gm., 3 grains, of the leaves, and 2 c.c., 30 minims of the tincture, is continued at four doses, four times a day until full digitalization is secured.

Another method recommended by Eggleston is the body weight method, by which it is claimed that the full digitalization can easily be secured in from 12 to 24 hours, and the valuable effect of the drug is reached within 6 hours. The total amount necessary is expressed in terms of the activity of the drug and the patient's body weight in pounds. The activity of the drug is determined by the cat method of Hatcher, the unit being the weight of the dry drug in miligrams, which is required to kill one kilogram of cat, when injected slowly and intravenously. The average total amount of digitalis required for oral administration to man is 0.15 of 1 cat unit per pound of body weight.

The following are Eggleston's formulas, and his explanation of them

$$\text{I} \quad \frac{\text{C.U.} \times 0.15 \times \text{W}}{1000} = \text{Grams of powdered leaf in total amount.}$$

$$\text{II} \quad \frac{\text{C.U.} \times 0.15 \times \text{W}}{1000} = \text{Cubic centimeters of tincture in total.}$$

$$\text{III} \quad \frac{\text{C.U.} \times \text{W}}{100} = \text{Cubic centimeters of infusion in total.}$$

In these formulas C. U. is the number of milligrams in one cat unit, and W is the patient's body weight in pounds. The following example illustrates the use of these formulas. A patient weighs 150 pounds and the digitalis available has an activity of 100 miligrams to the cat unit. Applying formula 1 for the powdered leaf, we have $100 \times 0.15 = 15$, $15 \times 150 = 2250$, $2250 \div 1000 = 2.25$ grams of leaf in total amount. Formula II gives $100 \times 0.15 = 15$, $15 \times 150 = 2250 \div 100 = 22.50$ cubic centimeters of tincture in the total amount.

To allow for individual variation, and idiosyncrasy of the patient, about 1/2 is given at the first dose, about 1/4 or a little less is given six hours later, and after another 6 hours about 1/6 to 1/8 of the total is given. Thereafter additional doses of about 1/10 of the total may be given at 6 hour intervals until the desired digitalization is secured. It is claimed that 6 hour intervals between doses allows time for complete absorption of each dose before the next is given, and therefore permits the certain avoidance of serious intoxications. It is claimed that the method is safe if the following precautions are observed.

Administration should be stopped on the appearance of nausea or vomiting, if the heart rate falls to or below 60 per minute, and if any evidences of minor intoxication appear. This demands definite observation of the patient and questioning by a skilled nurse or the physician before each succeeding dose, after the first dose is given.

The early evidences of the actions of digitalis in the graphic records is prolongation of the auricular ventricular conduction time. This is also one of the most common phenomena of digitalis action where there is a normal sinus rhythm present. In the electrocardiagram flattening or inversion of the T wave in leads 1 and 3 is nearly as constant as the prolongation of the P R interval. Digitalis may also produce a sinus arrhythmia in a previously regular heart or exaggerate a preëxisting one. None of these actions may be considered as definitely toxic, they indicate, however, a definite action from the absorption of the digitalis. The following signs and symptoms, however, indicate immediate cessation of the drug: nausea or vomiting, marked grade of sinus arrhythmia, especially when phasic in type, or when independent of respiration; the occurrence of partial or complete block; the occurrence of premature contractions not previously present; the coupling of the beats of the heart, that is an extra systole following each regular beat; the auricular ventricular disassociation, with or without the idioventricular rhythm; the occurrence of auriculo-ventricular or nodal rhythm, or auricular standstill; or any combination of the above irregularities.

Eggleston recommends to modify the body weight method of dosage as follows: if the body weight of the patient is unknown, and must be guessed at, for the first three doses to give 3/4 of the calculated amount, followed by 1/10 of the full amount at 6 hour intervals. If the cat unit strength is unknown of any given preparation of digitalis, calculate it as of 100, that being the average for high grade digitalis, but under these circumstances only give 3/4 the amount as calculated for the first three doses. If the patient has been taking digitalis during the previous ten days, if with graphic and electrocardiagraphic evidence there remains no signs of digitalis action, if the patient's condition is urgent, the method should be followed without modification. If it is not urgent, it is best to give only 75 per cent. of the calculated amount in the first three doses. If there be any evidences of previous action of digitalis only 1/2 the calculated amount should be given in the first 3 doses, if however, under these circumstances, the condition is urgent 3/4 of the calculated amount should be given.

The body weight method is specially recommended in urgent cases demanding immediate relief. If the case seems of great urgency, and injections of ouabain or strophanthin are decided upon, in spite of its dangers, if no digitalis has previously been given within 10 days, 1/2 to 1 milligram or 1/25 of a grain of ouabain may be injected, or 3/4 to 1 milligram of amorphous strophanthin, 1/80 to 1/60 of a grain. These doses may be repeated twice within the succeeding 24 hours if necessary, and it is better to use but 1/2 of the initial dose for repetition. If the patient has received digitalis within 10 days, the full dose as given above may be given, but never more than 1/2 its amount in succeeding doses. If there are any evidences of previous digitalis action present, the dose of ouabain should not exceed 1/250 of a grain, or 1/4 of a milligram, or 1/125 of a grain of strophanthin, or 1/2 a milligram, and in subsequent doses this should be cut in half.

Oftentimes in the chronic cardiac conditions it may be wise to contime small doses of digitalis over long periods of time, months or even years. This should be done in doses of from 1 grain to 2 grains of the leaves in 24 hours, either in a single dose, or 1/2 the dose at night and 1/2 in the morning or given as 10 to 20 to 30 minims of the tincture. Even this may be too much for some patients sensitive to the drug, and an excellent equilibrium can be kept in the hearts of some patients by giving 5 or 6 minims of the tincture once a day. This is particularly true of elderly people sensitive to the effects. The desired effects of digitalis as shown in the clinical improvement are seen in the subjective feeling of the patient in their relief from dyspnoea and cough and the disappearance of the sensation of palpitation or precordial distress; also the relief of the nausea produced by the abdominal congestion. There is also evident relief of the cyanosis and of tenderness over the liver, and increase in the urinary output, the disappearance of the edema, and the consequent rapid loss of weight, the diminution in the pulse rate, and the diminution in the pulse deficit, if it has been present.

This description of digitalis therapy is given as the definite instructions for those wishing to carry on the vigorous large dose digitalis therapy, which has recently been recommended. It cannot be carried out, and should not be given unless the physician can see the patient between doses or have the patient under such skilled control that the wisdom of giving each dose may be properly valued. Digitalis poisoning can come on extremely quickly and be of very serious import, and it may be vastly more serious than the degree of heart failure which one may be attempting to relieve.

Other Heart Stimulants.—Among other drugs that are used in heart failure is caffein, which increases the systolic contraction of the heart through stimulation of the heart muscle, but which may increase the wakefulness of the patient. It is used also for its diuretic effect, but this is of uncertain occurrence due to the fact of most patients being habituated to its use, and the morning cup of coffee is of more value to them as a diuretic than the dosage of caffein sufficient to make them restless and keep them awake. The effect of caffein in combatting sleep is exhibited in patients not only in that it prevents them from going to sleep but also in producing broken rest as the result of waking frequently during the night or waking early in the morning, thereby adding to the discomfort of the patient.

Theobromin and theophyllin are often recommended as diuretics, the former in doses of 10 to 15 grains, 3 or 4 times a day, and the latter as a grain and a half to 3 grains at similar intervals. With active kidneys and but little renal change they sometimes act well, especially if in accompaniment with digitalis therapy; in the majority of patients, however, they fail to act unless digitalis is given. Strychnine is frequently given, but as a stimulant of the nervous tissues, and beyond the nervous stimulation of the heart and general stimulating effect, it does not seem to have much action. The much vaunted cactus or cactin has in the hands of the writer never done any patient harm, nor any patient good; it seems to be fully inert. Spartein acts like aconite and not like digitalis; it should be used instead of aconite, and not instead of digitalis.

Hypnotics.—Often the restlessness, discomfort and unhappiness of the patient can be helped and ameliorated by hypnotic drugs. For these Mackenzie suggests ammonium bromide, 20 grains every four hours. It is sometimes of great benefit. Chloral hydrate is an excellent hypnotic, but in individual cases can produce intense mental depression, which in these patients prohibits its use. Of the newer hypnotics trional is sometimes of use to some patients, given particularly with milk or with food, and some hours before the desire to sleep is expected. The more easily soluble barbituric acid group under the names of medinal and veronal produce sleep, but usually pervert the personality of the patient, and are responsible for the peevish unhappiness and ill nature and meanness of many patients, the patient, however, being given full credit for a display of ill nature and unreasonableness for which the drug is entirely responsible. This hypnotic not infrequently causes patients to take unreasonable dislikes to individual members of their family.

It is claimed that the newer preparation of barbituric acid with the objectionable toxic radicals replaced by other chemical radicals, sold under the name of allonal, does not have this effect. It seemingly does not in such an intense degree, but when it is being used the patient should not be blamed for all exhibitions of unreasonableness or bad temper. Paralhyde is a valuable drug, but is a disagreeable drug to take because of its taste, and because of its offensive odor, which it gives in the patient's breath next day.

Opium and morphine or codein are valuable adjuncts to relieve the unhappiness, the strain, and the fear with which these patients are often dominated. Codein added to the trional is often very effective in producing sleep and relieving distress; morphine, particularly if pain be present, is invaluable, but the constipation that the opium group produces is a detriment, and in chronic patients it must always be remembered that the continued use over two or three weeks of small doses may bring with it the habit craving when they are cut off. Small doses of powdered opium given with the digitalis is often of great benefit.

Anti-luetics.—In the treatment of syphilitic heart diseases, mixed treatment may be given, or prolonged doses of iodide alone, or if in urgent cases, where it is believed that the heart failure is due to this form of infection, small doses of salvarsan should be given at 5 day intervals, followed by injections of mercury on the other days. By small doses is meant 1/10 of the usual dose, not more; 2/10 of the usual dose is a large dose of salvarsan to be given to a patient suffering from syphilis of the heart or of the aorta. The immediate bad effects are sometimes not seen, but in from 3 to 6 weeks after a full dose of salvarsan, sudden death is a danger that must always be remembered. Small doses, however, repeated for 4 or 5 times at 5 day intervals and then withheld for 2 or 3 weeks, and *mercury and iodide continued, will obtain a very satisfactory* response in the improvement of the cardiac condition. This method of salvarsan with the intramuscular injections of 1/8 of a grain of bichloride of mercury into the buttocks once a day between the salvarsan gives excellent results where there is acute heart failure in syphilitic hearts. The bichloride of mercury is more evenly absorbed than the salicylate of mercury and can, therefore, be better controlled.

The Arrhythmias.—The treatment of the arrhythmias when they dominate the picture in chronic myocarditis deserves special mention. Auricular fibrillation is the most frequent of the cardiac arrhythmias, and it is a condition in which digitalis has been most successful. A rapid digitalization of the patient with the auricular fibrillation is advisable if the patient shows marked evidences of heart failure. Often fibrillation will be present without a severe degree of heart failure being evident. The degree of digitalization, and also the value of the digitalis used, may be judged by the use of the pulse deficit as a criterion; under digitalis the pulse deficit rapidly diminishes and disappears, and if there be no diminution following digitalis it is evident that the digitalis has become inefficient or is unavailing. When auricular fibrillation has become permanent, sufficient digitalis should be given to keep the pulse at 70 or a little under, and the amount necessary to keep it there varies with the individual patient.

Recently the use of quinidine has been advised in auricular fibrillation. The best method of its dosage is to give from 3 to 6 grains of the neutral sulphate as a preliminary dose to test the sensitiveness of the patient to the cinchona group. If the administration is to be continued, 6 grains 3 times a day before meals has been found to be the most advisable amount. It is inadvisable to give more than 30 grains (2 grams) in 24 hours. The rhythm of the heart has become regular on the second or third day of the treatment when this treatment produces the desired effect.

Unpleasant symptoms such as palpitation, headache, diarrhoea, nausea and vomiting, abdominal pain, and buzzing in the ears have been occasionally noted; and a few cases also of collapse and death following its use have been reported. It is a drug that should not be given unless its effects can be closely watched. In the electrocardiograms taken impure flutter and real flutter of the auricle have been demonstrated as transitional mechanisms. Reversal of the direction of the T wave in the electrocardiogram and prolongation of the P R interval have also been observed. Intra-auricular block has also been reported as following the administration of quinidine.

The results obtained have been variously reported by different individuals. In the most favorable statistics 50 per cent. of the patients show either no effect whatever, or only a transitory increase in the rapidity of the auricular rate and an increased tachycardia.

In auricular fibrillation of recent occurrence and in paroxysmal fibrillation quinidine seems to be more effective than in those of longer duration; but even in some of these cases there is only a temporary relief from the arrhythmia, and the patients go back again to their cardiac irregularity. When it does act well and the cardiac rhythm is normal the drug can be discontinued while digitalis usually has to be continued. The exact proportion in which quinidine will be of value or the exact type of patient in which it is to be used has not yet been worked out, as it is of too recent recommendation. Different observers have reported different results and there are many cases of very favorable reports. It seems clinically wiser to give digitalis first, and if not successful to try the quinidine, as there is less danger of the injurious effects if digitalis has been given. In older cases of the chronic type, as seen in hospital patients in the writer's wards in Bellevue Hospital, in 35 consecutive patients quinidine produced absolutely no results, in the 36th patient it caused a rapid disappearance of the auricular fibrillation. Others, however, have reported very favorable results, especially when the fibrillation is of recent origin.

Auricular flutter occurs under the same causes as fibrillation, and it is best treated by digitalis.

The paroxysmal tachycardia has usually shown no response to digitalization. Wenkenbach recommends the use of quinine in premature contractions, and as a paroxysmal tachycardia is a continuous succession of premature contractions it would seem advisable to use quinine or quinidine in attacks of this form of tachycardia, giving 6 or 7 grains or 0.5 gm. a day in divided doses.

Heart Block.—In partial heart block, especially where the Stokes-Adams syndrome is increasing, it has usually been found that digitalis is contraindicated. There is a danger of increasing the frequency of the Stokes-Adams syndrome; however, in cases of partial block without the periods of unconsciousness it would be well to use the digitalis if the ventricles show the danger of cardiac failure through dilatation. In complete heart block, however, where the danger of Stokes-Adams syndrome is less, the digitalis may be of value as a means of increasing the vigor of the cardiac contractions and for this the full digitalis effect is not needed.

In cases of pulsus alternans the full digitalis effect is certainly not required, but the tonic effect of digitalis on the heart muscle may be used with benefit, and in these cases the small doses long continued are the ones that should be tried.

Sudden Heart Failure.—Where there is sudden heart failure and sudden collapse, and with apparent death of the patient, the intracardial injection of epinephrin has been used, and cases have been reported in which the heart has been made to go on after it had apparently ceased. This injection is without danger, and is best done by inserting a needle 6 to 10 centimeters long into the fourth left intercostal space near the sternum, just above the 5th rib. The needle is pushed about 1 or 2 centimeters straight in at right angles, and then turned slightly towards the median line and pushed further in to about 4 or 5 cubic centimeters. Some blood is immediately aspirated by the withdrawal of the piston, and the injection made, using a cubic centimeter (15 minims) of 1/1000 solution of epinephrin. Movements of the needle due to cardiac contractions are considered favorable. This method is also recommended in resuscitation of the newborn, and a few drops of the 1 to 1000 adrenalin solution is recommended. Using this method of procedure the technique here recommended avoids the mammary artery and the pleura, and goes directly into the right ventricle. This is recommended in sudden death from angina or sudden cardiac failure from any cause.

Prognosis.—The prognosis of the mild degrees of acute myocarditis in the vast majority of cases is perfectly good; it does not affect the course of the infectious disease or influence it for ill. In some cases of typhoid fever, however, and in typhus fever the breakdown of the heart occurs through the acute degeneration of the muscular fibers; in these cases it may cause a very serious and grave prognosis.

In diphtheria from 20 to 30 per cent. of the patients show cardiac complications; of these that show this myocardial degeneration 1/3 die, but that does not give the prognosis in any given individual case. Looked at broadly, one can see, however serious the case, the chances are two to one that they will recover. In patients that are apathetic, somnolent, with intense vomiting, and show bradycardia, the prognosis is always very grave. With the sudden appearance of complete heart block in diphtheria, the prognosis is also very grave. In pneumonia patients with a temperature over 103, Mackenzie states, that with the occurrence of extra systoles he has never seen a patient recover. While always a sign of bad prognosis, a few patients, however, do recover that show this sign, and while extra systoles appearing suddenly in the active period of infectious diseases indicate a condition of the myocardium that increases the severity of the prognosis, extra systoles during convalescence from these same diseases do not indicate any such gravity of prognosis.

During pneumonia the rhythms of fibrillation, flutter and arborization block increase the gravity of the prognosis in this disease.

In rheumatic endocarditis, the younger the patient, the more serious is apt to be the cardiac involvement, and with the pericardium involved the prognosis is more grave than when it escapes. With the myocardium involved to such an extent that it produces the contraction and scars producing a mitral stenosis, the prognosis takes on the prognostic significance of that endocardial involvement. The prognosis is in direct ratio to the seriousness of the stenotic condition, as evidenced by the presence and increase of the mitral diastolic murmur.

In general, acute myocarditis is a condition which is self-limited, and tends to recovery, the prognosis is good, but in rheumatic myocarditis, the disease tends to recur, and the recurrence brings on the continued involvement which, with each successive attack, makes more grave the outlook.

With evident syphilitic involvement of the heart and the aorta, the outlook is more favorable than often the symptoms would justify, for it is a condition that yields to treatment, and the prognosis in these cases would be directly proportional to the improvement under the specific medication.

With the acute myocarditis accompanying the acute endocarditis, the prognosis is entirely a matter of the prognosis of the endocardial involvement.

Of the influence of the rhythms on prognosis, it may be said that fibrillation and flutter are always signs of damaged heart muscles, and while it may be possible to keep them in check, the prognosis depends upon the readiness with which they answer to the control of digitalis, and also in the proportion in which the general circulation is maintained in spite of their presence.

The pulse deficit is also a useful criterion as to the improvement or failure to improve after any attack, but the general equilibrium of the circulation is really the point of prognostic value.

In paroxysmal tachycardia in younger people that does not go on to the break down of their general circulation the prognosis is not serious; only in the conditions of those attacks in which the equilibrium of the general circulation breaks down is the prognosis serious.

The prognosis in heart block is more serious with partial heart block, and the Stokes-Adams syndrome, than with the complete block and the idioventricular rhythm. While complete heart block does not seem to cause an immediate break down of the circulation, it necessarily limits the patient's activities and increases the seriousness of the prognosis regarding the length of existence, but does not necessarily mean a sign of immediate danger.

Alternation of the pulse is looked upon as of very serious prognostic import; if it occurs after some sudden physical strain or an acute morbid change in the myocardium, it is of less serious prognostic significance than if it occurs in the chronic conditions; and it is evidence of myocardial degeneration when it occurs in the few beats following the extra systoles. When alternation is associated with high blood pressure and with nocturnal dyspnoea it is of very serious import.

Arborization block, in which any portion of the bundle may be blocked off, may indicate a serious prognosis, because it indicates usually a general damage to the myocardial tissues, which having occurred once may readily occur in other portions of the conducting system, and is an expression of extensive arteriosclerosis or extensive myocardial replacement. If accompanied with arteriosclerosis, the prognosis is not as good as if it is of syphilitic origin, because the general arteriosclerotic condition of non-syphilitic origin is more apt to cause further blocking of any of the coronary vessels, and the coronary thrombosis of the vessels occurs, which is so common a source of sudden heart failure and death.

The irregularities of the heart action occur more often in syphilis than in any other one disease, and may or may not be amenable to treatment, depending upon the extent of the damage done which cannot be repaired, though the increase in rapidity of further damage may be materially lessened.

In general, in spite of the usually accepted idea, syphilis of the heart in its early stages is very amenable to treatment, and therefore possesses a much better prognosis than is usually believed.

In the chronic myocardial degeneration of chronic myocarditis with hypertension, however, the prognosis varies in proportion to the ability through general care of the patients, and to control the hypertension, and it varies also in ratio to the intensity and frequency of the attacks of intercurrent acute infections, which add their danger to the chronic condition. In all chronic forms of cardiac changes, the acute intercurrent infections control more the immediate prognosis of any given case than the chronicity, or the kind of morbid change which is progressing.

Janeway found that in these patients with the arteriosclerotic and chronic connective tissue replacement, and with the cardionephritis, that when properly cared for, and the equilibrium of their general existence and their circulation carefully watched, their chances of living to 58 years in men and 61 in women were fairly good.

Janeway found that neither the degree of blood pressure elevation nor the symptoms of onset were of any significance for prognosticating the duration of life. In this type of patients the greatest number died of gradual cardiac insufficiency, the second greatest of uremic convulsions, and the third largest number of apoplexy; of those patients that showed cardiac pain, the greater majority died from cardiac failure, and 1/3 of those showing pain died in an attack of it.

In the cardionephritic type, particularly in those in whom the height of diastolic tension is over 100, and who show a predominance of the nephritic element, the prognosis varies according to the insufficiency of the kidneys, rather than the insufficiency of the heart muscle.

Most patients will recover once from an acute breakdown due to acute disease superimposed on the chronic. But in patients over 60 years of age the acute cardiac breakdown from influenzal infection carries with it a serious prognosis.

Comparing the relative prognostic value of the various symptoms, the dilated right ventricle with bronchitis and emphysema does not carry with it as serious a prognostic significance as with dilatation of the liver, and the congestion of the stomach and abdominal viscera.

Occupation among those who earn their living by physical exertion has a great influence on prognosis. With a serious rheumatic involvement, the prognosis of a patient having severe physical exertion in his daily life will be greatly improved if he can change his occupation to that of work requiring milder physical effort. It may mean that he will be able to carry on his existence and be of economic value, rather than a chronic hospital patient from continuous attacks of heart failure.

In a city clinic, among those who earn their living by physical work, one is impressed by the saying that "rum, tobacco and stairs" are the three enemies of these patients. In the chronic rheumatic endocarditis and myocarditis from which many of these patients suffer, it is noticeable that overindulgence in tobacco has often brought about and increases the liability of their break downs. Alcohol adds also its danger in the same line, and stairs may be said to be the synonym for acute overexertion, or overexertion of any kind.

Many of these patients have learned in a heart clinic at Bellevue Hospital to accept the warning contained in this homely adage and have changed their existence of hospital invalidism into economic self-support by a change of occupation, and by care and diminution of overexertion, and by care of their personal hygiene. They also have learned the value of the subjective symptoms of early cardiac distress; by taking digitalis on Friday night, and sacrificing a half day's work on Saturday, continuing their digitalis until Monday morning, and if necessary resting in bed, they are fit again to go on with their work and keep themselves in economic independence.

The prognosis, therefore, of many chronic cardiac patients, especially those who are young, suffering from the acute strain of the rheumatic type, varies directly as their willingness to accept the restrictions which the disease carries with it, and also their willingness to make their damaged heart perform only what it can up to the limit of its capability.

The prognosis in all forms of the chronic type, therefore, depends upon the willingness of the patient to accept the restrictions of his eating, drinking and smoking, and the willingness of keeping the cardiac muscle in as good training as it can be kept physically. The prognosis varies also, according to the accidents of the acute intercurrent diseases with their injury and the intensity of the circulatory breakdown they produce.

The question of prognosis frequently arises in cardiac diseases in regard to marriage and pregnancy. Sexual intercourse is one of the severest strains that can be put on the heart in the chronic arteriosclerotic type of degeneration or in any forms of myocardial degeneration, if the cardiac balance as shown by attacks of pain or dyspnoea is in unstable equilibrium. It is very frequently the cause of acute heart failure and sudden death in elderly men. In acute cardiac conditions, with the heart in unstable equilibrium, the same danger may arise in either sex. Pregnancy is well borne in cardiac conditions, endocardial or myocardial, which are in stable and nonprogressive condition. This gives a bad prognosis for the mitral stenosis lesion with an early diastolic murmur and a myocardium which shows evidence of beginning heart failure. Under these conditions, pregnancy endangers the mother and should be terminated. If there are increasing evidences of heart failure from any cause during pregnancy, the question of termination of the pregnancy should be considered.

Pathology.—In acute myocardial degenerations or intoxications following infectious diseases, and in acute alcoholic poisoning, or following burns, there is an albuminous degeneration of the muscle fibers, which in the milder conditions is difficult to distinguish from the myocardial degeneration due to postmortem changes.

There is a deposit of albuminous granules between the fibers, sometimes so abundant as to conceal the striations of the fibers. It produces a dirty appearance of the myocardium, which is flabby and easily torn. In extreme instances there is a homogeneous clumping of the muscle fibers and a complete destruction of their structure, with the corresponding abolition of their function. This occurs in diphtheria and in other intense cases of myocardial degeneration, in typhoid fever, and sometimes in the acute pyemic infections. In the septic infections there may be added acute emboli which produce localized necrosis.

In acute conditions this necrosis, usually of infectious origin, goes on to localized suppurations. These occur in consequence of the secondary infections of influenza, or of scarlatina, diphtheria, typhoid fever, or gonorrhea, or may be associated with the ulcerative forms of endocarditis.

These small abscess areas are usually circumscribed, and consist of pus cells, broken down muscle tissue, and bacteria. These abscesses may open into the pericardium, setting up purulent pericarditis, or into the cavity of the heart, giving rise to thrombi of the heart and infective emboli in different parts of the body. The wall of the heart itself may rupture because of these abscesses, or an aneurysmal sac may form, or abscesses in the intraventricular septum may rupture, causing an opening between the two chambers.

In rare cases the patients may recover, and the contents of the abscesses become dry and be surrounded by the wall of fiber tissue, or the contents being absorbed, be replaced by a fibrous scar.

The fatty degeneration of the heart consists in the appearance in the muscle fibers of deposits of fat, or closely allied substances collecting in small droplets, sometimes few in number, sometimes so abundant as to almost entirely replace or conceal the normal striations; in very intense degree, the appearance of the heart has a universal yellow color, but usually the yellow appearance is in streaks or in patches, and is often best seen on the papillary muscles. The fatty infiltration occurring in obese people is different from this condition. The sub-pericardial fat may be increased to such an extent that it forms a thick envelope enclosing the entire heart, sometimes the accumulation of fat extends into the walls of the heart between the muscles, causing their atrophy to such an extent, even as to interfere seriously with their function. The fatty infiltration usually is not to this excessive degree, and is not sufficient to cause death, even in the fat patients.

These acute conditions recover leaving more or less scar tissue, or they may go into the chronic type of myocarditis showing brown atrophy of the myocardium.

In acute rheumatic endocarditis, a characteristic condition in the myocardium is present, this is the presence of the Aschoff bodies, which consists in a perivascular collection of cells of an epithelial type, with large nuclei, some of these elements resemble plasma cells, but are not probably examples of this type, others are of very large size, and resemble giant cells, with them occasionally are found eosinophilic and neutrophilic leucocytes. Although these small bodies are found in the connective tissue, they sometimes increase in size to such an extent, or are so abundant, that they involve also the adjacent muscle fibers. And these Aschoff bodies are specially abundant in the wall of the left ventricle near the base, and in the intraventricular septum. While these are characteristic of rheumatic infection, they are said not to be found in all cases.

Syphilis of the heart, if congenital, shows an acute diffuse fibrosis, with localization of the characteristic spirillae. Although this is of congenital origin, it is continued on into adult life as an interstitial myocarditis as shown by Warthin. This type of involvement is distributed about the arterioles and capillaries, which show very little vascular change.

In the heart of infants dying of congenital syphilis, not only is the interstitial increase well marked, but also with extensive loss of muscular fibers, and the spirochetes can be demonstrated in large numbers within the myocardium.

Brooks in studying 1000 consecutive protocols of autopsies was struck with the frequency with which syphilitic changes were found in the heart. In 50 consecutive cases of unquestioned syphilis, the cardiac lesions were studied in detail, 47 show unquestionable changes in the heart, and in over half of these series, death resulted from diseases of the cardio vascular system: 24 cases of cardiac involvement are reported in the secondary state of the disease, although the condition is not usually recognized until well into the tertiary stage, and of 300 cases, 276 came under observation only late in the third stage. In 200 cases it was shown that the patients had come for treatment relatively early in adult life, the average age for women being 38.1, and for men 44.75.

In the 50 cases above mentioned, it was shown that the syphilitic lesions originated and progressed most frequently from the terminals of the coronary system, which showed every phase of arteritis; 44 cases showed definite myocardial changes, although many of the lesions could not be definitely said to be syphilitic, they resulted from the syphilitic changes in the coronary vessels. Gummata of the heart were found in 5 cases, endocarditis in 37, in 17 of these the mitral valve was involved, as well as the aortic, and in 7 the aortic valves only were involved.

Usually with syphilitic endocarditis the conus arteriosus is involved, and noticeably, as was emphasized by Allbut, the floor of the sinuses of valsalva, that is the aorta at its junction with the heart.

Two aneurysms of the sinus were found, the pericardium was involved in 28 cases, directly due to syphilitic involvement, or indirectly due to the changes of the coronary arteries.

The chronic lesions of myocarditis are really those of a fibrous hyperplasia, rather than of a genuine inflammation. In the hypertrophied heart, produced by the hypertension and continued increased overaction. there is a connective tissue increase as well as an enlargement of the muscular fibers themselves. Most observers do not believe that there is an actual increase in number of fibers, although Bruno claims to have shown an actual muscular fiber increase.

There is no correspondence between the pathological findings in chronic myocardial conditions and the clinical symptoms of cardiac insufficiency; the myocardial changes in the muscle tissue may be those of chronic brown atrophy due to the chronic intoxications, or the chronic result of lack of recuperation from the degeneration of acute disease or the acute degeneration from infection added to the chronic degeneration already present. The amount of replacement hyperplasia seems to be more in proportion to the arterial degenerations which have taken place, in the connective tissue, except of course, in a few instances, in which the connective tissue scarring is the result of previous acute myocardial degeneration. Hypertrophy of the contracting cardiac muscles appears to be a physiologic growth in response to increased demands of work, whether from increased tension or damaged valves. The contracting muscles retain vigorous function as long as they are properly nourished or are undamaged by chronic intoxications, such as renal retention or intestinal absorption, or by acute infectious degeneration.

Dilatation of the heart occurs when there is required a larger ventricular cavity, as in aortic regurgitation, or when the morbid processes within the muscle fibers themselves remove or diminish the normal power of these fibers to stretch and contract as increased work is thrust upon them. Heart failure comes on as the stretching and contracting power of the muscles wanes.

The lesions in the coronary arteries, such as an obliterating endarteritis with or without thrombosis or emboli, lead to degeneration or necrosis of the muscle with acute inflammation of the fibrous tissue. This occurs in small foci or diffuse areas. This hyperplasia in chronic arteriosclerosis may occur more abundantly in the muscles supplied by capillaries than by small arterioles, and the muscle fiber may remain less degenerated surrounding the smaller blood vessels themselves, and more marked in the areas of capillary destruction.

The separation functionally of the conducting from the contracting system of the heart has focused the attention of pathologists on the special pathology of the conducting system.

Monckeberg in a review of the present knowledge, reports that in certain cases of sudden death, in which the lesions found in the contracting system were insufficient to account for the sudden heart failure, finds that in a certain number of cases there have been found sufficient pathological destruction of the tissues composing the conducting system to justify the deduction that death was due to the lesions found only in the Purkinje system. In cases following acute infectious diseases, seen chiefly following diphtheria, among the lesions found are those of acute hemorrhage, destroying the Purkinje fibers, mechanically displacing, tearing or injuring them.

Subendocardial hemorrhages were found also in measles, tuberculous meningitis, apoplexy, hemorrhagic pachymeningitis, etc.

These hemorrhages were also found in tetanus and eclampsia, and Ribbert reports also cases in these last two diseases of degeneration of the bundle fibers without the presence of hemorrhage.

The most frequent lesions found after diphtheria are those of fatty degeneration, which must be differentiated from a normal fatty infiltration, which is commonly found in the conducting system, as well as in the remainder of the heart.

Monckeberg insists that there must be an actual demonstrable destruction of the specific fibers of the conducting system connected with the deposits of fat before any deduction of causal relationship between the evidences of clinical injury and the lesions found is justifiable.

Tanaka found an almost complete isolation of the bundle only once in 15 cases, 5 times the degeneration was more marked in the Purkinje system, that in the myocardium, 3 times less so, and 4 times practically equal involvement of the myocardium and the specific system.

Berblinger found the isolated degeneration of the conducting system only once in 8 cases, but in several instances, the degeneration was so much more intense in the Purkinje system than in the myocardium that he deemed the term "system disease" justifiable

Roemer claims that in diphtheria the bundle lesions are in a measure independent of the myocardial changes, and diffuse lesions of the Purkinje system are not a rarity.

In chronic diseases showing heart block, syphilis and rheumatism are the two most common infectious bases for the changes produced; numerous cases of gumma have been reported, and the chronic inflammatory changes of rheumatism have also caused, by its scar tissue, permanent damage to the conducting system.

In the chronic degenerations, as evidenced by brown atrophy, there has been a distinct variation in the degree of this change found occurring in the myocardium, and in the bundle fibers. Monckeberg again reports that in some cases the bundle showed a more intense degree of brown atrophy than the myocardium, and vice versa. In arteriosclerosis of the heart a definite differentiation between the lesions of the specific vascular supply to the bundle and the vascular supply of the myocardium have been reported.

One case in particular presented an intact bundle lying on an extensively and thoroughly scarred subjacent and surrounding tissue. These cases are sufficient to show a certain independence of injury, as well as of function, occurring between the two systems of the heart.

There seems to be an increasing tendency on the part of pathologists to ascribe certain occurrences of sudden death to lesions of the conducting system, independent of the morbid changes in the general myocardium.

Clinically, the more one studies the average circulation of the coronary system, as depicted in the recent work of Gross, one realizes how by the time the fourth decade of life has been reached, there is a definite increase in the vascular supply to the left ventricle relatively to that of the right, and the vessels themselves begin to show slight tortuosity, there is also a beginning noticeable increase in the anastomoses between the two coronary arteries occurring in the cardiac septum. There is also a noticeable increase not only in the amount of fat occurring on the heart, but also in the very minute arterial supply giving independent nourishment to this new tissue. By the time the sixth decade is reached, the average heart shows a very noticeable lack of minute capillary supply in the right ventricle, and a preponderating supply to the left, and also the beginning atrophy of the myocardial muscles and an increased tortuosity and arteriosclerotic changes in the vessels. These are average conditions, which means of course, that some individuals age sooner than others, and certain other individuals retain much more of their youthful tissues and cardiac circulation.

One's mind naturally connects these evidences of normal age changes with the physiology of cardiac function under exertion, and one realizes the justification for Bainbridge's saying, that the circulation of the heart itself was the weak link in the correlation between respiratory and the circulatory systems under increased exertion. The heart as it grows older evidently cannot supply through its vascular system the increased amount of blood necessary to give to itself the increased amount of oxygen. The coronaries have lost their resiliency and do not answer by dilation and increased function to the demands for rapid response to give increased systolic output per beat.

The normal increased output per beat of the heart is supplied from vigorous muscle fibers, supplied by actively functioning coronary vessels. This vascular supply is in the average person diminished as age goes on, and the normal reserve of the heart is naturally diminished with it. The changes in the vascular supply also explain the breakdown of the circulation in acute infections, such as pneumonia, for the right of the heart is the one most injured in its circulatory functions, and disproportionately injured by the ordinary changes taking place. They also show the foundation for the increasing frequency of heart failure in the chronic myocardial conditions, which have increased the connective tissue hyperplasias and the arteriosclerosis beyond that which even the average heart would show. They also indirectly emphasize the added dangers of the acute infections which injure the essential fibers.

The left ventricle still performs its function, even though these functions are greatly increased, due to the increased arterial tension increasing the blood supply and the nutrition of the muscular fibers, but we usually have not given due credit to the injuries which may predominate in the right ventricle.

As we stated in the beginning, we cannot explain the clinical symptoms alone on the pathologic lesions found, but we must translate it into terms of physiologic function to interpret the symptoms in both acute and chronic myocarditis.

SECTION V

DISEASES DUE TO PHYSICAL AGENTS

CHAPTER I

HEAT EXHAUSTION

BY L. C. JOHNSON, M.D.

Definition, p. 381—Etiology, p. 381:—Exciting causes, p. 385—Symptomatology, p. 385:—Clinical History, p. 385; Physical findings, p. 386; Laboratory findings, p. 387—Diagnosis, p. 387—Complications, p. 387—Treatment, p. 389—Prophylaxis, p. 389; General management, p. 389; Management of convalescence, p. 390—Prognosis, p. 391—Pathology, p. 391—Historical summary, p. 392.

Definition.—Heat exhaustion is a disturbance of the heat-regulating mechanism of the body, due to exposure to excessive heat, in an atmosphere with a high degree of humidity, and characterized by collapse, with or without a rise in temperature. In a healthy individual, there is the added element of muscular exertion, or of long hours of strain, mental work, or worry.

Etiology.—In discussing the etiology of this disturbance, it is well to consider briefly the underlying physiological principles of heat-regulation, and the experimental contributions which have been made.[1] The regulating mechanism for heat control is necessarily a complex arrangement, since it has to do with balancing heat production and heat dissipation, each of which processes involves several factors. Yet, in a healthy individual, there is a fairly constant end-result, under all conditions, namely, an almost constant body temperature. Heat production occurs very largely by the oxidative processes in the muscles. There is doubtless some heat generation in the abdominal viscera, but only a small portion of the total calories required are produced here, and the amount so generated is practically negligible. Heat loss is accomplished partially through the lungs, in the expired air, but mainly through the skin, by conduction, radiation, and evaporation of perspiration. These are purely physical processes, and the amount of heat so dissipated depends upon the clothing that is worn, the temperature of the air, the degree to which the air is saturated with moisture, and whether or not the air is still, or in motion.

Government, or balancing of the two processes, is brought about by the heat-regulating or thermogenic center, which is situated in the region of the optic thalami, or corpora striata. Whether or not there is a single center, or several closely related centers, is a matter for discussion, but is clinically of slight importance, since the relation between them is so intimate that they act as one. Barbour [2] has been able to apply heat and cold locally in the region of the thermogenic center. When heat is applied, there is diminished heat production in the body of the animal, with increased loss of heat. When cold is applied, there is general increased heat production, and decreased loss of heat. Puncture of this region produces marked elevation of temperature, as has been demonstrated by many physiologists since the time of Claude Bernard. The peripheral mechanism consists of afferent sensory fibers, and efferent vasomotor nerves which, by reflex action through the center, regulate the amount of blood in the capillaries on the body surface. There are also efferent fibers which control the secretion of perspiration. This appears to be an active secretory process, directly under nervous domination. Normally metabolism is increased with muscular activity, and the temperature of the body and of the blood is elevated from 1° to 4° F. (0.55° to 2.20° C.), according to the amount of exertion. Loss of heat is at once brought about by dilatation of the peripheral vessels, by radiation and conduction and, if this loss is insufficient, secretion of perspiration occurs, and the element of evaporation is introduced as a further means of heat loss.

An individual, to be able to endure high temperatures without the elevation of body temperature, must be able to perspire, and external conditions must be such that evaporation of perspiration is possible. Zuntz[3] describes the case of a man who had no sweat-glands. On exposure to heat, or when working in hot weather, his temperature rose at once to 102° F. (38.88° C.). The man had discovered, however, that if he wet his shirt from time to time, he was perfectly able to go about his work. This loss of heat by evaporation is evidently of prime importance in all cases of heat exhaustion. Haldane[4] says that when the evaporation of water from the skin is lessened, the loss of heat is inhibited. He places the limit of man's accommodation to moist heat, when stripped to the waist and sitting, at from 88° to 90° F. (31.11° to 32.22° C.), measured by the wet-bulb thermometer. If the man works, the limit is much lower. At 80° F. (26.66° C.), wet-bulb, there is rise in body temperature in a short time, the pulse becomes rapid, there is profuse perspiration, and exhaustion. Leonard Hill[5] has stated that high temperatures do not affect the body temperature, so long as loss of heat by evaporation is not disturbed. He considers it especially important that the surrounding air be in motion. In his experiments, young adults were placed in a closed chamber, at body temperature. They very soon became restless, but by starting a small fan, and merely keeping the air in motion, they were able to endure in comfort air which was overheated, moist, and chemically impure. The reports of the various army researches, American, British, and German, all note that men are better able to endure marches and heavy work in the tropics, or in summer, when there is a good breeze blowing.

Loss of heat is also dependent upon the amount of water within the body, which is available for perspiration. The body maintains its fluid supply at a fairly constant level, and a large reserve, which is readily available, is constantly carried within the muscles, according to Hunt.[6]

The percentage of water in the blood is not appreciably lowered, even after the loss of several liters of water as perspiration. He adds that if the reserve is extensively reduced, replacement occupies many hours, and that this delay is of importance. This is a strong argument against drawing on the reserve body fluids by restricting the fluid intake.

The experiments of Woodyatt[7] are of particular significance. He discovered that, by dehydrating animals by large intravenous doses of glucose solutions, it was possible to produce definite rigors, with fever as high as 108° F. (42.22° C.), which was relieved by bringing the body weight back to normal by the administration of water. It was not necessary for the fluids to leave the body, as the same results occurred if the fluids were fixed within the body by salts or protein. He could change the degree of fever at will, by changing the water level.

The amount of water lost is astonishingly large. In men exposed to the sun, either at work or at rest, at Aldershot, it was noted[8] that 4 men lost on an average three pints of water by perspiration on a march of seven miles. A man lying in the sand can lose 280 grams (266 c.c.) of water an hour by perspiration. It seems probable that in every case of heat exhaustion, there is a large initial loss of water (Aron[9], Wooley[10]). This depletion of the fluid reserve has a definite influence upon metabolism in general.

Heat exhaustion occurs in the greatest number of cases in the hot season of the year, but it may occur at any time, if an individual is exposed to heat associated with a high humidity, as is the case with cooks, laundry workers, stokers, and steel mill operatives. It is most common in low lands, which lie close to bodies of water, where protracted periods of heat occur, accompanied by high humidity, as for instance the Mississippi valley, the regions about the Great Lakes, and the eastern and southern sea-coasts. Less commonly cases are reported from higher elevations, and in high altitudes the condition is rare. Most cases occur in cities, where people are crowded together, and subject to unwholesome surroundings, bad habits, errors of diet, and bad hygiene in general. Those who are debilitated or convalescent from a severe infection or operation, are particularly prone to the condition. Moschcowitz[11] records several postoperative cases. Chronic organic disease, myocardial or renal insufficiency, prolonged nervous shock, strain or worry, all render an individual less able to withstand heat. The subject is of decided military importance, as in war men may be transported from a temperate to a tropical climate, and forced to unusual muscular activity for long hours in the sun. The natives are naturally better able to endure the heat in these countries, but even some of them succumb. They have, however, a dark skin, and do not need to resort to clothing to protect their bodies from the sun's rays. They perspire more readily and, being clothed scantily, have the advantage of greater surface evaporation.

Alcohol produces a diminished efficiency in temperature regulation, and after large doses of alcohol the normal reactions to heat and cold are inhibited. Weisenberg,[12] while on duty in the Philippines, observed heat exhaustion only rarely, even among newly-arrived troops, unless they drank alcohol in some form or other, and the reports of all army observers note the incidence of heat exhaustion as running parallel with the use of alcohol. In the cases of 25 patients of Gauss and Meyer,[13] who were questioned closely as to the use of alcohol, all but one had taken beer during the twenty-four hours previous to attack, and in amounts varying from a few glasses to a gallon.

Of these authors' 158 cases, 85 were laborers, 12, teamsters, 8, carpenters, 4, firemen, 3, laundry workers, 3, housewives, 3, cooks, and 3, clerks. There were 152 males, and 6 females. One hundred and sixteen were in the third, fourth and fifth decades, the majority of them being in the fourth. One hundred and two were foreigners, and only 45 were Americans.

The solar rays *per se,* are seldom an active cause of heat exhaustion. A white man exposed to the sun will suffer a diffuse erythema, later followed by pigmentation. If the exposed area is very large, he may have slight fever and malaise. But in the case of all whites the clothing worn is ample protection against the active rays of the sun, nor are the rays able to penetrate to any vital part of the body. Aron[9] exposed monkeys to the sun and found that they died if they could not accomplish heat loss. When only the head of the animal was exposed to the sun, with the body protected, the animal showed no ill effects even after long hours. Aron concludes that insolation of the skull of animals is without effect, if the body temperature is kept within normal limits. He adds that in the case of animals devoid of sweat-glands the sun's rays will, by radiation, heat the skin and subcutaneous tissues to temperatures incompatible with life. Finny[14] in India conducted a similar experiment, using rats as subjects, and found that when they were exposed to the sun in still air death occurred, but that if the air was kept in motion, the animals were unaffected. Wanhill[15] studied the temperatures of helmets worn by men exposed to the sun, to discover whether the color of the lining of the helmets had anything to do with the temperatures which developed. He concluded that the principal factor which affected the inside temperature was the ventilation of the helmet. Phalen[16] conducted experiments with 500 soldiers, who were clothed in orange-colored undergarments, and concluded that they were not any better protected against the heat than were the men who wore white underclothing. Chamberlain,[17] and Freer,[18] discussing the sunlight and its various rays, found that the ultra-violet rays were fatal to amebæ and bacilli, but Chamberlain concludes that it is very doubtful whether the actinic component of the sunlight is a factor in the tropical morbidity and deterioration of troops. He also observed that blondes withstood the heat fully as well as the darker skinned brunettes. It is moreover a common observation that the greatest number of cases of heat exhaustion among soldiers and sailors occurs, not while they are working in the sun, but at night or in the rest periods, when they are in the barracks, or below deck, where the air is moist and still, and the heat stifling.

Exciting Causes.—The disturbance of the heat-regulating mechanism is apparently brought about by a disturbed metabolism, associated with a lowered water level, in which there is retention of some toxic substance. Whether this substance is an acid or of protein origin, is not clear. Where there is increased muscular activity, the general metabolism is stimulated, with increased respiratory and nitrogenous exchanges, and a rise in temperature. If this is not relieved by increased heat loss, there is added excitability, which contributes to a vicious circle. Pembrey [19] draws attention to the fact that the secretion of perspiration is controlled by the chemical composition and temperature of the blood, and that if the nervous mechanism is paralyzed by some toxic substance, we may have increased vascularity of the skin, without perspiration. Wooley [10] believes that, with the initial loss of water which occurs in heat exhaustion, there is a concentration of the colloids of the tissues, and retention in the cells of substances which should be carried off. This may embarrass the cells to such an extent that there is an imperfect splitting of the protein molecule; hence the presence of the toxic portion of the protein molecule described by Vaughan.[20] Gordon [21] also suggests the possibility of such an intoxication. Gradwohl [22] believes that heat exhaustion is an intoxication, brought about by substances formed within the body, under abnormal conditions of heat retention. He emphasizes the similarity of heat exhaustion and uremic states. Mayer,[23] working with corals, thought it possible that death resulted from the accumulation of acid, possibly carbonic acid (H_2CO_3), in the tissues, the rate of formation of this acid being commensurate with the rate of metabolism of the tissues. The animals of the same class which have a high rate of metabolism, as measured by the oxygen consumption, are more sensitive to heat, and to carbon dioxid, than are those which have a low rate of metabolism. Mayer[23] believed that death occurring in the case of these animals, at high temperatures, was not due to asphyxia. Maud Menten [24] notes an increased hydrogen-ion concentration of the blood, when barometric pressure is low; we should encounter low barometric figures in heated air, both dry or moist, and in moist air when it is not overheated. Sambon [25] and Manson advanced the theory that heat exhaustion was due to infection with a specific organism, and termed the ailment siriasis. Their contentions have not held.

Symptomatology.—Clinical History.—The onset is almost always sudden, but frequently there are prodromal symptoms for a few hours or a few days before an attack. These consist in general depression, headache, malaise, dizziness, anorexia, nausea and vomiting, diarrhea, epigastric distress, restlessness, insomnia, and great thirst (polydipsia). Convulsions may be present, and the temperature may be normal, subnormal, or greatly elevated. Gauss and Meyer [13] cite the case of a driver who left his seat perfectly well, leaned over a fountain to get a drink, and knew nothing from that time until he awoke in the hospital. He had been admitted with a temperature of 110° F. (43.33° C.). Another man felt ill and restless at home, and went walking in the street for relief, where he was found unconscious. Others are found in a state of collapse in their beds. Blair[26] records notes on a case as follows:

> A woman aged fifty-four complained in the morning of slight malaise. She did her usual work in the kitchen, complained of thirst, and drank large quantities of water. The temperature of the kitchen was 91° F. (32.44° C.). At six in the evening, while sitting in the yard, she was taken suddenly ill. It was noted that her lips were pale, and that the veins of her neck were engorged. She breathed without difficulty, and her pulse was 100 per minute and of good quality. She spoke a few words intelligently, and then became incoherent, restless, irritable, and resisted examination. Her jaws were tightly closed, the pupils were dilated at first, but later contracted, and complete unconsciousness supervened.

Physical Findings.—The physical findings depend upon the degree of trauma. A patient suffering from collapse, without a tremendous initial rise of temperature, greatly resembles a person in a state of shock. He may or may not be unconscious; the skin is pale, cold, and clammy, and bathed in a profuse perspiration. The pulse is small, thready, and poorly sustained; the temperature is slightly elevated, or subnormal. Respirations are shallow, and there is often sighing. Blood-pressure (systolic) is usually low—90-100 mm. Heart-sounds are faintly heard, and reflexes may be elicited. The patient may usually be rallied from this condition and recover, or, within a few hours, show a marked elevation of temperature. Those who have suffered greater trauma are usually found unconscious, with a temperature well above 105° F. (40.55° C.). In the case of these patients the skin is hot, dry, and flushed. Some are conscious or stuporous, others may be delirious. Convulsions are frequent in this type, and may be tonic or clonic, and general or focal. Frequently a single extremity is involved, or the muscles of the face and neck. The pupils are contracted, but as the coma deepens they may be dilated. The reflexes are dependent upon the depth of the coma, and upon whether or not paralyses exist. In general, as the coma is lessened and consciousness returns, the reflexes also return, the superficial ones at first, and the deeper ones later. The pulse-rate corresponds roughly to the temperature. With a temperature of 110° F. (43.33° C.) or over, the pulse-rate is from 150 to 180, and with continued hyperpyrexia it becomes imperceptible. The respirations also vary with the fever; with a temperature below 105° F. (40.55° C.), respirations are from 16 to 30; above 107° F. (41.66° C.) they are from 30 to 60. Breathing in coma is labored, shallow, and sometimes grunting, or of the Cheyne-Stokes character. Bowel movements are almost always involuntary. Consciousness returns with a fall in temperature, and this may occur in a few hours, or be delayed for several days. The return to consciousness is frequently followed by a deep sleep.

In many cases, the prevailing symptoms, and main physical findings, are cramps and extreme contractions of the muscles, particularly those of the legs. Edsall[27] comments upon the large number of such cases seen among stokers in ships, or workers in metal, and notes that they are frequently described by ship doctors. In cases which he described, there were spasm and twitchings of the arm- and leg-muscles, later of all the muscles, which seemed to be extremely irritable, so that a slight stimulus brought on maximal contraction. This manifestation disappeared in twenty-four hours, and left the patient free, except for exhaustion. He believed that this was due to faulty metabolism within the muscles themselves, and not to central irritation. Weisenberg[12] describes the case of a cook, forty-one years old, with a history of alcoholism, who had such attacks, which never came except when he was at work in the kitchen. He was seized with violent cramps of various groups of muscles, lasting for three or four days, which were so severe that at one time a shoulder was dislocated by the contractions. He had previously suffered an attack of poliomyelitis, the muscles of his left leg showing the usual atrophy, loss of power and reflexes. During his attacks of heat exhaustion, these muscles were involved in the same manner as were those in which the nerves were still intact.

LABORATORY FINDINGS.—The laboratory findings are not characteristic, yet seem to indicate an intoxication of some sort, particularly those of the urine and blood. In 25 cases of Gauss and Meyer[13] the urine of all showed large numbers of hyaline and granular casts on the second day, but albumin was present in only 5 cases. Gradwohl[22] noted a marked parallelism between the urine and blood chemistry findings in heat cases, and in those of renal insufficiency. He agreed with Meyers and Lough[28] that cases having a high nitrogen retention, as evidenced by a creatinin determination of 5 mg. (0.0770 grain) per 100 c.c. of blood, were usually fatal. The white-cell count in the cases of Gauss and Meyer ranged from 7,200 to 15,000 per c.mm. The spinal fluid studied by Dopter,[29] Hublé and Pigache,[30] Dufour,[31] and Römer[32] showed an increase of cells, polymorphonuclear at first, but later mononuclear. The vomitus in a few cases contained blood, and in others there were bloody, mucous stools.

Diagnosis.—Diagnosis is comparatively simple where there is a history of exposure to excessive heat, a sudden onset, and signs of collapse or hyperpyrexia, without other cause. Undoubtedly many cases in which persons are found unconscious, with convulsions or paralyses, in the hot season of the year, and who pass rapidly into deep coma, and die, are diagnosed as cerebral hemorrhage or apoplexy, without the consideration of heat as the first cause. In the case of persons who have been confined to their beds for a long period, and who pass suddenly into collapse, the diagnosis of heat exhaustion may also be overlooked, and death attributed to some obscure cause which is never clearly determined.

Complications.—The complications are not numerous, and are most often present where the damage has been extreme. Immediately after return to consciousness there is sometimes *disturbance of speech,* and *inability to swallow.* Also for a time there may be *disorientation, hallucinations,* and *delusions.* Other patients show a sort of *negativism,* in which the attention may be arrested, but not held. A marked irritability is noted. Reid [33] mentions *pneumonia* as being a fairly common complication, frequently overlooked. Of 160 cases, he found this disease present in 10.7 per cent., and it was the cause of 20 per cent. of deaths. In cases of individuals suffering from renal insufficiency, where there is but a slight margin of accommodation, or tolerance for trauma, heat exhaustion is undoubtedly the cause of the complete renal insufficiency which ensues.

Sequelæ.—Many individuals show a permanently impaired ability to withstand high temperatures. Others are subject to headaches, vertigo, nausea and vomiting, on exposure to the sun. Impairment of memory, altered conduct and disposition, with mental degeneration, are not infrequent where the attack has been severe. Motor lesions are not uncommon, and there are fairly numerous records of hemiplegia, or of paraplegia. Disturbances of speech do not commonly persist, and ataxia is rare. Out of 435 cases Hiller [34] noted paralyses in 7. Goebel [35] notes as sequelæ: psychoses, neuroses, hysteria, paraplegia, hemiplegia, and facial palsy. Out of 40 cases, Pembrey[19] noted sequelæ in only 2. One showed absence of perspiration, and the other wasting of the muscles with ankle-drop. Weisenberg [12] reports the case of a patient who had fever for twenty-two days, and who was admitted to the nerve ward with mania, a month after his discharge from the hospital. He showed a marked ataxia, and his findings were those of a cerebellar lesion. Nonne [36] reported a similar case.

Clinical Varieties.—Several types have been described, but there seems to be little reason for a division into clinical types, since there is a single cause, and since the apparently different forms vary only in degree of disturbance, rather than in origin. It is not uncommon, moreover, for a case to be first seen as the less severely injured type, in which a high temperature later develops. It is, however, true that cases tend to fall into two classes. In one, which has been described as heat exhaustion, the onset is more gradual, and prodromal symptoms are always present; the temperature is seldom above 101° F. (38.33° C.) and frequently normal or subnormal; the pulse is small and easily compressed; the patient is usually conscious; recovery is frequently prolonged, but is complete and with no sequelæ. The second type has been described as heat stroke. The temperature rises to extreme heights, unconsciousness with convulsions is common, and few or no prodromata have been noticed. The pulse is rapid but of fair volume, respirations are often of the Cheyne-Stokes type, and recovery or death usually ensues within a few hours or days. With this type sequelæ have been commonly noted. It seems probable that the difference is largely one of degree, or that the individual who has rendered himself more susceptible, by errors of diet, or alcoholic excess, presents the more violent picture.[87]

Treatment.—PROPHYLAXIS.—Prophylaxis has to do largely with simple hygienic procedures. The **skin** should be **kept clean by frequent bathing**; the **diet** should be **light** and easily assimilated; the **clothing, light, loose**, and **airy**. **Alcohol** should be **forbidden**, and **tea, coffee**, and **tobacco** used very **sparingly**, since all may be vasomotor disturbers. Extreme **fatigue, worry** or **anxiety** should be **avoided**, and **heavy work** confined to the **cooler parts of the day**. **Houses** should be **well-ventilated**, windows open and shaded, and **fans** used where possible to keep the air in motion. **Rest** in the middle of the day should be encouraged, particularly for those who are under par physically. The **bowels** should be kept **regular**, and particular attention given to the **water** intake. Other **cooling drinks** may be used, but at least twelve or fifteen glasses of water should be taken in a day. Those who have suffered from an attack should resort to higher **altitudes**, or open places, where the **air** is **cool**, and dry. Those who live in cities during a long-continued hot period, should seek to lessen the usual daily tasks as much as possible and seek rest and recreation from the daily wear and tear.

GENERAL MANAGEMENT.—Where hyperpyrexia is present, the first consideration is to lower the temperature; **hydrotherapy** is the one effectual method of accomplishing this result. The patient should be placed in a tub of tap-water, and friction applied to the body; ice should be added to the bath freely, and the temperature taken rectally every minute. When the temperature has fallen to 102° F. (39° C.), which should occur in from ten to thirty minutes, the patient is to be wrapped in sheets, and removed to a bed, which should be located in a cool, quiet, airy place. The temperature usually continues to fall, and may reach as low as 95° F. (35° C.). If there is still elevation of temperature, an **ice-bag** should be applied to the head, and **cracked ice** given **by mouth**. For a temperature under 103° F. (40.45° C.) **sponge baths** may be given, but if it rises above 103° F., the patient should again be given tub baths. **Iced enemata** have been used by some physicians with success, while others consider them of doubtful value. **Stimulants** are employed freely and, as long as emergency exists, should be given hypodermically, or even intravenously. **Caffein-sodium benzoate**, grains 2 to 4 (0.130 to 0.260 gram), should be administered subcutaneously, and repeated every three hours, also **strychnin sulphate**, grain 1/30 (0.0021 gram), and repeated every three hours. It is sometimes of advantage to alternate the two, so that stimulation is received at short intervals. When the pulse is very rapid, **digalen** may be employed, or any digitalis preparation ready for hypodermatic use, in doses of 15 minims (0.92 c.c.) repeated every two to four hours, until 100 minims have been given, when the dose should be lessened. For intravenous use, a single dose of **strophanthin**, 1/120 grain (0.0005 gram), may be given, but should not be repeated for twenty-four hours. In extreme emergency, injections of **whiskey** or **ether**, 15 minims (0.92 c.c.), may be used, but the action is largely reflex, and they are not to be employed for continued cardiac stimulation. For convulsions, restlessness, or active delirium, **morphin** may be used, but sparingly, grain 1/6 (0.010 gram), hypodermatically, and repeated every three or four hours. **Sodium bromid**, grains 30 (2 grams), and **chloral hydrate**, grains 15 (0.972 gram), may be given by mouth, and repeated every four to six hours; it may also be given in milk per rectum. Where convulsions are severe, sufficient **chloroform** to produce full anesthesia may be necessary. This is sometimes continued for a prolonged interval.

In view of the findings of McKenzie and Le Count,[38] repeated **spinal puncture** should be of decided benefit; the interval between punctures must be regulated by the symptoms of the patient. **Antipyretics** of the coal-tar group are of doubtful value, and since the cardiac muscle is always damaged, they are to be avoided. For alcoholics, **whiskey**, ½ to 1 ounce (15 to 30 c.c.), with **paraldehyde**, dram 1 to 2 (3.75 to 7.50 c.c.), may be given, to prevent delirium tremens, and repeated in an hour if necessary.

The **diet** should be **liquid** at first, and fluids should be urged upon the patient. **Milk, orangeade** and **lemonade**, 6 ounces (178 c.c.), should be taken every two hours, and where the patient is unable to swallow, **proctoclysis**, with **glucose**, and **sodium bicarbonate**, 5 per cent. of each, should be employed, by the drop method. If desiccation is extreme, **normal saline solution**, 13.5 to 17 ounces (400 to 503 c.c.), may be given intravenously, or by hypodermoclysis, administered slowly. Lewis and Packard,[40] in some of their cases, withdrew from 10 to 15 ounces (295.70 to 444 c.c.) of blood, and replaced this with normal saline. They considered this procedure of doubtful value. Particular attention should be directed toward elimination, and the bowel tract is frequently the only avenue left open. For this purpose **saline cathartics**, or **compound jalap powder** may be used. **Pilocarpin** is **not** to be used to bring about sweating, and the stimulation of the skin by external heat should be resorted to only in cases where there is no fever. Blood chemistry determinations should be performed, to check up for retention of nitrogen bodies. Where there is no fever, the treatment is largely stimulative. The patient should be wrapped in **warm blankets**, **massaged**, or external heat applied, if the temperature is subnormal. The stimulative procedures outlined above are to be employed, and the matter of elimination watched very carefully. If fever occurs later, it is subject to the same treatment.

MANAGEMENT OF CONVALESCENCE.—In convalescence the patient should have a **light, nourishing diet**, and should be kept in bed until the pulse and temperature have been normal for at least forty-eight hours. He should be cautioned against any exposure to heat, and if possible should spend a period of time **away from his usual surroundings**

and duties. For paralysis and other nervous involvement, **massage,** with **active** and **passive motion,** proper **exercises,** and **electrotherapy,** may aid in recovery.

Prognosis.—Of the 158 patients of Gauss and Meyer,[13] 63 died, and of these 46 had a temperature of 105° F. (40.55° C.) or above on admission. One hundred and twenty-nine were in a state of coma on admission, and 58 of them died without regaining consciousness. Thirty-five had a temperature of 101° F. (38.33° C.) or lower on admission, and of these 10 died.

Recovery depends upon the extent of trauma, and upon the general condition of the patient at the time of attack. With proper treatment, the number of deaths among soldiers is surprisingly small, while in the case of older individuals living in cities, the percentage of deaths is considerably larger. Gradwohl [22] observed that those patients whose symptoms were severe, but whose blood showed a low nitrogen content, recovered, while those who had high retention died, even though their symptoms were not alarming at the time of admission. The direct cause of death is not demonstrated, but Pembrey [19] believes that it has to do with changes in the nervous mechanism and the heart, or in the respiratory mechanism. Marinesco [41] describes changes in the Nissl substance of the nerve-cells, and Halliburton and Mott [42] found that the globulin of the nerve-cells coagulated at 42° C. It is possible that death may be due to partial coagulation of these cells.

Pathology.—McKenzie and LeCount,[38] in a study of 37 cases which came to autopsy comparatively soon after death, report edema of the brain in 22 cases, edema of the leptomeninges in 9, and of both, in 4 cases. There was marked general passive hyperemia, especially of the brain and lungs, hyperplasia of the spleen, cloudy swelling of the liver, kidneys, and myocardium. The mucous membranes and the skin, particularly over the sides of the thorax in the axillary region, showed petechial hemorrhages. The suprarenal cortices showed the yellow material to be irregular and lessened in quantity; in one case fresh hemorrhages were noted in the substance of the pons, and in another, small softenings of the lenticular nuclei. The spinal fluid in all was clear, colorless, and usually increased in amount. The investigators determined the water content of a series of nearly normal brains, taken from individuals who died suddenly and by accident, and placed the average water content of brain tissue at 80 per cent. In the heat cases of 1916, the water content of the brains varied from 81.16 to 83.78 per cent. but in the few cases of 1917, the water content was slightly above, or below, the normal figure. They figured that, since the brain is enclosed in a rigid case, even a slight increase, of 1 per cent., would be sufficient to subject the brain to considerable pressure. They explained the lessened water content in the brains of the 1917 cases by the fact that there were fewer cases admitted, and that they received more effective treatment in the wards than was possible with such a very large number of cases the previous year. When the brains were hardened in formalin, and examined, the ventricles were found to be enlarged; under the microscope the sections gave evidence of edema, and the blood-vessels were crowded with red blood-cells. The authors emphasize as significant findings the enlargement of the spleen, and the edema of the brain. Sensfftleben[48] records the findings of a soldier who died on the march, as follows: The post-cerebral veins were dilated, and full of blood; dural and pial hemorrhages were present. The basal vessels were empty, but the lateral ventricles were full of blood, as were also the vessels of the choroid plexus. Most of the pathological reports do not reveal any more significant findings, and as Pembrey pointed out, some minute work very soon after death should be done, in order to locate the pathological evidence, if it is to be found.

Historical Summary.—In going over the literature it is particularly interesting to note the terms under which the syndrome of heat exhaustion has been described. Until recently the sun's rays themselves have been considered to be a large factor, or a direct cause. "Sunstroke," "insolation," "Sonnenstich," "calenture," "ictus solis," "thermic fever," "siriasis," "heat apoplexy," "heat asphyxia," "heat stroke," "heat prostration," and "Hitzschlag" are terms which have been applied, and they are a fair summary of the events which have been observed, and of the causes to which the disturbance has been attributed. As far back as 1775, important experiments were conducted by Blagden and Fordyce, which have been recorded anew by Pembrey.[19] These experimenters remained in closed rooms, and after a short period of time, took the temperature of the mouth, and of the urine passed. They found they could remain in a room filled with dry air, heated to 239.9° F. (115.49° C.) and remain for fifteen minutes, without any elevation of temperature. They placed water in two jars and poured a layer of oil over the surface of one of them. They noted that the water in this vessel began to boil, while the temperature of the water in the other vessel did not rise above 172° F. (77.9° C.). After staying in a room of moist air, at a temperature of 129.9° F. (54.5° C.), for 15 minutes, they observed that the body temperature was elevated to 100° F. (37.5° C.). These are simple experiments but pertinent, and we find them only in retrospection.

REFERENCES

1. MacLeod, J. J. R. Physiology and biochemistry in modern medicine. St. Louis, 1918. C. V. Mosby & Co.
2. Barbour, H. G. Die Wirkung unmittelbarer Erwärmung und Abkuhlung der Warmezentren auf die Korpertemperatur. Archiv. f. Path. u. Pharmacol. Leipzig, 1912, lxx, 1.

   Barbour, H. G., and Wing, E. S. The direct application of drugs to the temperature centers. Jour. Pharmacol. and Exper. Therap. (Bolt), 1913, v, 105.
3. Zuntz and Schumberg. Studien zu einer Physiologie des Marsches. 1901, p. 311.
4. Haldane, J. S. The influence of high air temperatures. Jour. Hyg., Cambridge, 1905, v, 494.

5. Hill, L. Recent advances in physiology and biochemistry. London, 1908. Address to the Physicians' Sec. Assn. for Advancement of Sc., Section J., 1912.
6. Hunt, E. N. The regulation of body temperature in extremes of dry heat. Jour. Hyg. Cambridge, 1912, xii, 479.
7. Woodyatt, R. T. Studies on intermediate carbohydrate metabolism. Harvey Lectures, 1915-16.
8. Committee on Physiological Effects of Food, Training and Clothing on the Soldier. 2nd and 4th Reports. Jour. Roy. Army Med. Corps, 1909, xii, 211; Ibid., xiii, 592.
9. Aron, H. Investigation on the action of the tropical sun on men and animals. Philippine Jour. of Sc., 1911, vi, 101.
10. Wooley, P. G. Insolation; its prophylaxis and treatment. N. Y. Med. Jour., 1914, xcix, No. 24, 1165.
11. Moschcowitz, A. V. Postoperative heat stroke. Surg., Gyn. and Obst., Chicago, 1916, xxxiii, 443.
12. Weisenberg, T. H. Nervous symptoms following heat stroke. Jour. Am. Med. Assn., 1912, lviii, 2015.
13. Gauss, H., and Meyer, K. A. Heat stroke; a report of 158 cases from Cook County Hospital. Amer. Jour. Med. Sc., 1917, cliv, 554.
14. Finny, C. M. Sunstroke, or heat stroke. Indian Med. Gaz., 1918, liii, 361.
15. Wanhill, C. F. Factors which may influence the production of heat stroke among the troops on the march. Jour. Roy. Army Med. Corps, 1914, xxii, 661.
16. Phalen, J. D. An experiment with orange-red underwear. Philippine Jour. Sc., 1910, v, 525.
17. Chamberlain, W. P., and Vedder, E. B. The effect of ultra-violet rays on amebæ, and the use of radiations in the sterilization of water. Philippine Jour. Sc., 1911, vi, 383.

——— Observations on the influence of the Philippine climate on white men of the blond and brunette type. Philippine Jour. Sc., 1911, vi, 427.

18. Freer, P. C. The tropical sunlight. Philippine Jour. Sc., 1910, v, 1.
19. Pembrey. Heat stroke. Jour. Roy. Army Med. Corps, 1913, xxi, 156; Ibid., 1914, xxii, 629.
20. Vaughan. Protein-split products, in relation to immunity and disease. 1913, Lea & Febiger.
21. Gordon, A. Osler's Modern Medicine. Sec. Edit., 1914, ii, 332.
22. Gradwohl, R. B. H., and Schisler, E. A study of thermic fever, with special reference to the blood and urine chemical findings. Amer. Jour. Med. Sc., 1917, cliv, 407.
23. Mayer, A. G. Is death from high temperature due to accumulation of acids in the tissues? Amer. Jour. Physiol., 1917, xliv, 581.
24. Menton, M. The alkalinity of the blood in malignancy and other pathological conditions, with observations on the relation of the alkalinity of the blood to barometric pressure. Jour. Cancer Research, 1917, ii, 179.
25. Sambon, L. W. Not heat fever but an infectious disease. Remarks on the etiology of sunstroke. Brit. Med. Jour., 1898, i, 744; Ibid., 1899, ii, 650.
26. Blair, M. A. Notes on a case of heat stroke, of the hyperpyrexial type. Lancet, 1911, ii, 1550.
27. Edsall, D. L. A disorder due to exposure to intense heat. Jour. Am. Med. Assn., Dec. 5, 1908, p. 1969.

——— Two cases of violent but transitory myokymia, and myotonia, apparently due to excessive heat. Amer. Jour. Med. Sc., 1904, cxxviii, 1003.

28. Meyers, U. C., and Lough, W. G. The creatinin of the blood in nephritis: Its diagnostic value. Arch. Int. Med., 1915, xvi, 536.
29. Dopter. Bull. et mém. Soc. méd. d. hôp. de Par., 1903, xx, 1396.
30. Hublé, M., and Pigache, R. Sequelles nerveuse consecutives au coup de châleur. Arch. de Neurol., Paris, 1908, ii, 265, 263.

31. Dufour, R. . Des resultats de la ponction lombaire dans l'insolation. Revue neurol., Paris, 1909, xvii, 317.
32. Römer, C. Über die Pathogenese des Sonnenstichs. Monatschr. f. Psych. u. Neurol., Berlin, 1915, xxxvii, 85.
33. Reid, W. D. Pneumonia not a rare complication of heat prostration. Boston Med. and Surg. Jour., 1912, lxvii, 217.
34. Hiller, A. Der Hitzschlag auf Märschen. Berlin, 1902.
——— Wesen u. Behandlung des Hitzschlages. Deutsch. med. Wchnschr., 1913, xxxix, 1185.
——— Zur Pathogenese des Hitzschlages. Berlin klin. Wchnschr., 1907, xliv, 939.
——— Hitzschlag und Sonnenstich. Leipzig, 1917, Thieme.
35. Goebel, A. J. L. Über die Nachkrankheiten des Hitzschlages. Berlin, 1905, O. Francke.
36. Nonne. Akute Ataxie nach Überhitzung. Deutsch. med. Wchnschr., 1907, l, 868.
37. Bram I. The treatment of sunstroke and heat prostration. N. Y. Med. Jour., 1914, c, 570.
38. McKenzie, P., and LeCount, E. R. Heat stroke, with a second study of cerebral edema. Jour. Am. Med. Assn., 1918, lxxi, 260.
39. Norton, H. R. Sunstroke during the summer of 1896. N. Y. Med. Jour., 1897, lxv, 311.
40. Lewis, M. J., and Packard, F. A. A report of 92 cases of thermic fever treated at Pennsylvania Hospital in the summer of 1901. Trans. Assn. Amer. Phys., 1902, p. 409.
41. Marinesco, G. Récherches expérimentals sur les lesions des centres nerveux consecutive a l'insolation. Compt. Rend. Acad. d. Sc., Paris, 1906, cxliii, 853.
42. Halliburton, W. D., and Mott, F. W. The coagulation temperature of cell-globulin and its bearings on hyperpyrexia. Arch. Neurol. Path. Lab., London Co. Asylum, Claybury, 1903, ii, 727.
43. Lambert, A. Heat stroke. Ref. Handb. of Med. Sc., N. Y. 3rd Edit., 1915, v, 124.
44. McClure, W. B., and Sauer, L. W. Clothing as a factor in the production of heat stasis. Amer. Jour. Dis. Child., 1915, ix, 490.
45. Simpson, R. J. S. Humidity and heat stroke. Jour. Roy. Army Med. Corps, 1914, xxiii, 1; Ibid., 1908, xi, 441.
——— The solar element in heat stroke, in its physical relations.
46. Ogilvie, W. H. Sunstroke. A heresy. Jour. Roy. Army Med. Corps, 1912, xix, 444.
47. Revenstorf. Hitzschlagkranke. Deutsch. med. Wchnschr., 1907, xxx, 868.
48. Senfftleben. Über die Entstellung des Hitzschlages. Berl. klin. Wchnschr., 1907, xliv, 775, 807.
49. Sutton, H. The influence of high temperatures on the human body, especially with regard to heat stroke. Jour. Path. and Bact., Cambridge, 1908, xiii, 62.
50. Van Giesen, I. Pathology of insolation. Med. Rec., N. Y., 1900, lvii, 1134.
51. Weiner, E. Hitzschlag und Sonnenstich. Wien. klin. Wchnschr., 1915, xxviii, 721.
52. Duncan, A. Remarks on some recent theories on the action of heat in the tropics. Jour. Roy. Army Med. Corps, 1908, xi, 71.
53. Steinhausen, F. A. Nervensystem und Insolation. Berlin, 1910.
54. Koidzumi. Ztschr. f. Mil. Aezte, Tokio, 1918, lxxv, 5, 24.
——— China Med. Jour., Shanghai, 1917, xxxi, 336; Ibid., 1918, xxxii, 573.

CHAPTER II

MORBID CONDITIONS DUE TO CHANGES IN BAROMETRIC PRESSURE

By Joseph W. Schereschewsky, M.D.

Introduction, p. 395—Conditions due to compressed air, p. 395:—Work in compressed air, p. 395; Physical laws to which compressed air workers are subject, p. 397; Respiratory requirements of the body at atmospheric pressure, p. 397; Law of partial pressure, p. 398; Volume of air required in compressed air work, p. 398; Description of compressed air illness, p. 402; Cause of compressed air illness, p. 407; Prevention of compressed air illness, p. 411; Treatment of compressed air illness, p. 423; Devices for safety and comfort of workers, p. 425.

Conditions due to diminished barometric pressure, p. 426:—Symptoms of mountain sickness, p. 427; Types of mountain sickness, p. 428; Cause of mountain sickness, p. 430; Prevention of mountain sickness, p. 443; Bibliography, p. 444.

Introduction.—The sea of atmosphere surrounding the earth, at the bottom of which we live, exerts a pressure at sea-level of approximately fifteen pounds to the square inch. We are not conscious of this pressure because the tissues of the human body like water are practically incompressible and the pressure of gases in the interior of the hollow viscera and of bony cavities, such as the middle ear and the frontal sinus, is the same as that of the exterior. Man is exposed to greatly increased barometric pressure when working in compressed air, and to greatly decreased barometric pressure when climbing high mountains, in aeroplane flights, and in balloon ascensions.

CONDITIONS DUE TO COMPRESSED AIR

Work in Compressed Air.—The hazards of working in compressed air may be looked upon as a most important occupational hazard, because of the direct danger to the worker, when the needful measures for his safety are neglected, and because the opportunities for injury are increased by the great development of the engineering feats of the day, such as the construction of massive bridges over deep bodies of water, the driving of underwater tunnels, the sinking in watery soil of the foundations for our towering office buildings, the increasing use of the diving dress in salvage operations and to secure pearl and sponge from the ocean floor.

Because bitter experience has shown that exposure to the increased barometric pressure incident to these operations carries with it the risk of acute illness, permanent disability or death, whenever the pressure or time of exposure exceeds certain limits, it is highly necessary to understand the causes of this morbid action, and to know the principles by which they may be prevented or relieved.

Workers are subjected to increased barometric pressure in pneumatic caissons, in the driving of subaqueous tunnels, and in the use of diving bells and of diving suits. The following brief description of each of these kinds of work will serve to give the requisite idea for understanding the conditions met with.

PNEUMATIC CAISSONS.—The use of pneumatic caissons is recognized as the most reliable method for the sinking of important foundations or piers, either under water or in water-bearing soil.

Generally speaking, a pneumatic caisson is a device for sinking foundations to firm ground through various distances of water, quicksand, silt and other watery soil. It is a box-like structure of steel, concrete or heavy timbers placed upside down in the location where the foundation for the pier or other work is to be sunk. In this way a closed chamber is formed of which the ceiling and walls are the airtight roof and sides of the caisson, and the floor the soil through which the caisson is to be sunk. The lower edges are usually bevelled, so as to form cutting edges, which aid the sinking of the caisson.

Air-locks.—In order to allow workers to pass in and out of the caisson, and to provide for the removal of excavated materials, spaces are left in the pier masonry containing shaft provided with "air-locks." These air-locks are chambers, usually cylindrical, either at the top or the bottom of the shafts with doors in opposite ends, one opening into the compressed air space and the other into the open air.

The process of entering the caisson, or "locking in," is as follows: The door leading to the compressed air space being closed, the worker enters the air-lock. The outer door is then closed and compressed air admitted into this air-lock through a valve until the pressure in the lock is equal to that in the compressed air space. The caisson door is then opened and the worker enters. In leaving the caisson, or "locking out," the process is reversed.

SUBAQUEOUS TUNNELLING.—The driving of tunnels beneath bodies of water has been among the most conspicuously successful under-water engineering feats of recent years. The principle employed is the same as that in sinking pneumatic caissons—*i. e.*, air-pressure keeps the water from entering at the tunnel-head—but the work proceeds in a generally horizontal instead of a vertical direction.

DIVING-BELLS.—Diving-bells are cylindrical or thimble-shaped chambers of iron or steel. They are open at the lower end, contain benches or supports for workers, and may be lowered to various depths of water. Light is furnished either by thick glass windows or by electric light. The water is prevented from rising into the interior of the bell by means of air-pressure.

NAKED DIVING.—Naked diving is still extensively in use among primitive people, in sponge and pearl fisheries. Naked divers are usually trained in their profession from childhood. According to Hill, mothers hold their children under water at an early age in order to develop their powers of resistance.

Considering that the lungs are filled prior to their descent with air at atmospheric pressure, naked divers penetrate to depths which seem astonishing. From sixty to seventy feet is a usual descent. In some instances a depth of from one hundred and twenty to one hundred and thirty feet has been attained.*

---

* G. Musenga reports an instance of a diver who reached eighty meters without the aid of diving apparatus.

Diving in Diving Suits.—In the diving suit, the same principle is employed as in the pneumatic caisson, viz., the air pressure within a waterproof garment which is attached to a metallic helmet is varied, by means of an air pump at the surface, so as to counterbalance the external hydraulic pressure.

The diving suits usually employed in this country consist of seven parts as follows:

1. a metallic dome-shaped helmet furnished with heavy glass windows, connection for air hose and outlet valve, secured by a segmented screw to a metallic breast plate. This in turn is attached by clamping devices to
2. the waterproof diving suit,
3. flexible air hose with metallic couplings,
4. leaden weights which are suspended from the back and chest,
5. weighted shoes,
6. life line,
7. air pump.

The diving suit permits the carrying on of extensive and complicated submarine operations. Through its use and with proper precautions, diving to great depths has been accomplished. Thus, in the salvaging of the United States Submarine F–4 in Honolulu Harbor, depths of over 300 feet, subjecting the divers to ten atmospheres of excess pressure, were attained.

Physical Laws to Which Compressed Air Workers Are Subject.—It is evident from the foregoing description of compressed air work that the physical conditions to which all compressed air workers are subjected are fundamentally the same, and differ from work at ordinary atmospheric conditions only because of the increase in barometric pressure.

Respiratory Requirements of the Body at Atmospheric Pressure.—It is a familiar fact that air as inhaled in the lungs is a gaseous mixture consisting approximately of 79 per cent. nitrogen, 20.98 per cent. oxygen and 0.04 per cent. carbon dioxid. The average composition of expired air is 79 per cent. nitrogen, 16.02 per cent. oxygen and 4.38 per cent. carbon dioxid. The air has therefore lost 4.94 parts of oxygen and gained 4.34 parts of carbon dioxid. The discrepancy between the oxygen lost and the carbon dioxid gained is due to the fact that a certain portion of the oxygen combines with hydrogen and forms water.

The total air capacity of the lungs is in the neighborhood of from 4,000 to 5,000 c.c. In normal breathing the tidal air is about 500 c.c. The average resting adult requires about 1/4 cubic foot of air per minute. This requirement rises rapidly with physical exertion. A man at moderate physical labor requires in the neighborhood of 1½ cubic feet of air per minute.

Before inspired air can reach the air-cells of the lungs it must first pass through and fill the nose, throat, windpipe and bronchial tubes. The capacity of these is about 140 c.c. The ventilation of the air-cells is therefore accomplished for the most part by diffusion between the alveolar air and the tidal air. For this reason expired air, as it issues from the nose and mouth, does not correspond exactly with the composition of the air in the alveoli of the lungs, which contain considerably more carbon dioxid—in the neighborhood of 6 per cent.

Law of Partial Pressure.—The passage of gases in and out of the body is governed by the well-known law of partial pressure. This law is, briefly: If a mixture of gases exerts a certain pressure, each gas of the mixture exerts a pressure proportional to the percentage of the gas present in the mixture. If air is approximately 1/5 oxygen and 4/5 nitrogen, it follows that, at the ordinary atmospheric pressure of 15 lbs. to the square inch, the pressure exerted by oxygen is 3 lbs., and that by nitrogen is 12 lbs. In similar fashion, in alveolar air, which contains about 6 per cent. of carbon dioxid, the partial pressure due to the carbon dioxid present is approximately 6 per cent. of 15 lbs. or 0.9 lb.

Observation and experiment have shown that it is the partial pressures of oxygen, nitrogen and carbon dioxid, and not the percentages, which are of importance so far as vital processes are concerned. Thus, if we progressively rarefy air we effect no change in its percentage composition, yet animals will rapidly succumb as soon as the partial pressure of oxygen is reduced below a certain limit. On the other hand, a much lower percentage of oxygen than is normally present in atmospheric air will sustain life if the partial pressure due to the oxygen is raised by compressing the mixture.

In similar fashion the percentage of carbon dioxid present in alveolar air reacts to increases in barometric pressure. If we increase the atmospheric pressure to which we are exposed by going into compressed air, either in caissons or below the surface of water in a diving suit, the percentage of carbon dioxid in the alveolar air will diminish proportionally to the increase in the pressure. Thus, exposure to an atmosphere of 15 lbs. excess or of 30 lbs. absolute pressure will have the effect of diminishing the carbon dioxid in the alveolar air from 6 to 3 per cent.—since 3 per cent. of carbon dioxid in a gas mixture at 30 lbs. absolute pressure exerts the same partial pressure in pounds as 6 per cent. at 15 lbs. absolute pressure.

Volume of Air Required in Compressed Air Work.—The need for the maintenance of a constant tension of carbon dioxid in the blood and tissues of the body, and as a consequence in the alveolar air, leads to the following important conclusion (first pointed out by Haldane) in regard to the air supply to be furnished workers in compressed air: The volume of air which must be furnished each individual is the same, measured at that pressure, as would be required by that person at atmospheric pressure, so that at no time will the tension of carbon dioxid in the alveolar air be greater than that corresponding to 6 per cent. divided by the absolute pressure in atmospheres.

Effect of Compression on the Worker.—It is only while the pressure is changing that a person under excess barometric pressures feels symptoms. As the gauge rises, there is a sensation of pressure in the ears which may become acutely painful if communication between the rhinopharynx and middle ear is not free. The pain has been compared to the sensation caused by forcibly introducing a stick into the ear canal. It is due to the fact that the air-pressure on both sides of the eardrum has not been equalized. If the communication between the middle ear and rhinopharynx is not speedily opened, a rupture of the eardrum is likely to follow.

Compressed air workers themselves recognize the necessity for a free channel of communication between the middle ear and the pharynx. Beginners are instructed to swallow hard and frequently, or to make forcible expiratory efforts with the mouth shut and the nose held.

Pain may also be felt in the other bony cavities of the skull, such as the frontal sinus and maxillary antrum. Such symptoms are most likely to occur in workers suffering from acute or chronic catarrh.

The inability to equalize the pressure in the interior of the cavities is known to compressed air workers as "blocking," or being "blocked." Persons who are subject to chronic catarrhs are poorly adapted to compressed air work, as the swollen mucous membranes prevent free access of air to these cavities. Compression may give rise to intolerable pain, and there may be hemorrhages from the nose and ears because of the cupping effect.

As the air-pressure rises there is usually a sensation of warmth due to the fact that air when compressed becomes hot. Therefore, if the air is not properly cooled as it enters the air-lock, the temperature may rise considerably.

There is very little effect upon the pulse and the respiration, except that the respirations are slightly diminished in number. There is practically no effect upon the blood-pressure or the circulation.

Many observers have noted that caisson workers become thin and anemic, and some have explained this fact on the theory that the air-pressure drives the blood out of the skin and mucous membranes to deeper parts of the body. While it seems probable that the number of red blood-cells does become slightly diminished as a result of work under compressed air, the pallor and loss of weight is in all likelihood principally due to another cause. The temperature of the interior of caissons is likely to be high, because of the heat given off in the compression of the air. Moreover, the conditions are usually such, because of excavations in watery soil, that the air of caissons is saturated with moisture. Besides this, compressing the air itself increases its relative humidity. Thus air 50 per cent. saturated with vapor will be 100 per cent. saturated if compressed to an additional atmosphere; and air 33 per cent. saturated will be 100 per cent. saturated if compressed to two additional atmospheres. Workers are therefore frequently exposed to high heat combined with a high degree of humidity. This is likely to be followed by the loss of appetite and weight and the characteristic pallor common to all who work under similar conditions.

As the pressure increases the voice is said to take on a peculiar nasal quality. The inability to whistle as the pressure reaches two or more atmospheres has been noted by many writers. This is due to the fact that, owing to the greater density of the air, more force is required to produce vibrations. This inability to impress vibrations on the air also gives rise to sensations of slight numbness about the lips. In compressed air the sense of smell is also said to lose something of its keenness. This is not due to any loss of the sensitivity of the nose, but to the fact that owing to the greater density of the atmosphere, more resistance is offered to the escape of particles from odorous substances.

Many workers express a feeling of greater lightness and ability to perform muscular feats while under pressure, complaining of lassitude and fatigue on decompression. It is thought that these sensations are subjective, and not due to any quality resident in compressed air. Former writers have ascribed these sensations to stimulation of metabolism because of the increased tension of the oxygen in the air. Experiments, however, have shown that the presence of an increased amount of oxygen has no practical effect upon the rate of metabolism.

While the oxygen in chemical combination with the hemoglobin of the blood shows no material increase, there is naturally an increase in the amount of oxygen in simple solution in the blood-serum, sufficient to keep the blood in the veins from becoming dark. Venous blood in persons subjected to increased barometric pressure is, therefore, bright red, similar to the arterial blood.

Owing to the diminution in volume of gases in the intestines (which, of course, are at atmospheric pressure at the beginning of compression), a slight lessening of the abdominal circumference is noted during compression, so that the belt may be drawn up to an additional hole.

When once the air in the bony cavities of the body (middle ear, sinuses of the skull) has become equalized to the caisson pressure, the worker is entirely unconscious of the compression. Respiration and muscular movements are just as free as at atmospheric pressure. Hill states that when he and Greenwood were compressed in an experimental chamber to 92 lbs. excess pressure, a degree of pressure far in excess of that to which caisson workers have ever been subjected and only occasionally supported by divers, there were no subjective symptoms whatever due to the great increase in barometric pressure.

ACCIDENTS WHILE UNDER COMPRESSION.—Caisson workers in general and divers in particular are naturally subject to certain peculiar accidents which are the direct outcome of the increased air pressure to which they are subjected. Thus, in caissons, in the event of sudden failure in the air-pressure, due to bursting of the air supply pipe, the water may rise suddenly in the caisson and drown the workers before they have a chance to escape. Again, caissons have exploded, causing fatalities. In tunnelling work, where the tunnel is driven in loose silt, "blow outs" have been known to occur, the compressed air escaping under the front edge of the shield up through the river bed in such quantities that the air-pressure cannot be maintained. Unfortunate workers have been caught in the rush of air and blown out through the river bed.*

Divers are subjected to serious accidents. If the air supply fails, or the air hose bursts, air may suddenly be driven out of the suit, and suffocation or a dangerous or fatal "squeeze" from the outside water pressure may occur.

"Squeezes."—"Squeezes" are among the accidents to which divers are subjected, and in all diving operations great care must be used to avoid them. In general a "squeeze" is caused by any substantial excess of the water pressure over the air pressure, and may be brought about in various ways. Consider, for instance, what would be the result if a diver were suddenly to fall a distance of from 20 to 30 feet, either into an unexpected hole in the bottom, or down the hatchway of a submerged ship, and his air supply were not increased proportionately to the rapidity of his fall. The diving suit, as previously described, consists of an incompressible copper helmet and breast-plate, and a collapsible rubber suit. A fall of 30 feet will add an excess pressure of 15 lbs. to every square inch of the body. If, therefore, there were no increased pressure to the air supply to counterbalance this suddenly applied pressure from the outside, the air would be driven from the collapsible suit into the helmet. If the difference in pressure occasioned by the fall were not greater than could be counterbalanced by the compression of the air in the helmet due to the added volume driven

---

* This is said to have occurred, without causing injury, to a worker in the course of the construction of the original Hudson River tube.

in from the suit, no serious harm would result. If, however, this equality were not produced, the outside pressure would tend to drive the diver into his helmet, thus possibly producing severe or fatal injury. A fall of 20 feet, when the diver is working in comparatively shallow water, will produce more serious effects than when he is working at greater depths, for the resulting increase in pressure will be proportionately much greater when compared to the original pressure in shallower than in deeper levels. Thus, a fall from 33 to 55 feet would have the effect of raising the excess pressure in the proportion of 15 to 25. A similar fall, from 165 to 187 feet, would increase the pressure only as 75 to 85. In the first instance, the diver would be subjected to pressure nearly 1.66 times greater than the original pressure; in the second instance, the pressure is only 1.13 times greater.

*Asphyxia.**—Asphyxia is a result of insufficient air or of failure of the air supply.

Accidental Blowing Up.—Through sudden increase in the air supply, or failure of the outlet valve to work, the suit becomes filled with air, the diver becomes lighter than the water, and tends to rise rapidly to the surface. This may cause harm in several ways. If the diver is blown up from a considerable depth, serious compressed air illness may result, or he may be injured by colliding with floating bodies.

Fouling.—The lifeline may become entangled in submarine obstructions, and thus prevent the diver from ascending. In this way, exposure to a high atmospheric pressure may be prolonged beyond the limits of safety. The situation usually requires that another diver descend and clear the diver who is fouled.

Mechanical Injuries from External Violence.—These are of many kinds and may happen in various ways.

Exhaustion.—Deaths from exhaustion in diving have occurred. It is probable that an inadequate air supply has been a factor in some instances.

Drowning.—French states that there are 2 cases of drowning on record. In both instances the helmet became detached. There is no danger of drowning because of a rent in the suit. So long as the air-pressure is maintained in the helmet, water cannot enter it. If the escape valve is closed completely,† air will enter the suit and force down the water, the excess escaping through the rent.

Oxygen-poisoning.—In the course of his investigations, Paul Bert found that when animals were exposed to a very high atmospheric pressure or to a lower pressure of pure oxygen, the high tension of the oxygen acted as a poison on the animal. It was thrown into spasms, and became stiff (like a piece of wood, as Bert described it), so that it could be lifted by a hind leg. These effects were observed whenever the tension of the oxygen was 2 or 3 atmospheres.

In addition to this, J. Lorrain Smith has shown that high pressures of oxygen, even though insufficient to produce convulsions, acted in a strongly irritant manner on the lungs, producing congestion and pneumonia. He found that exposure to an oxygen tension of 40 per cent. of an atmosphere for eight days had no effect; 80 per cent. of an atmosphere killed 2 mice in four days, which after death showed congestion of the lungs, while 2 mice survived unharmed. An average oxygen pressure of 1¼ atmospheres killed mice in an average of sixty-four hours, 1.8 atmospheres in twenty-four hours, and 3 atmospheres of oxygen produced inflammation of the lungs in five hours. His results were confirmed by Hill.

---

* The following description of the accidents to which the divers are subjected is based upon statements made by French.

† With some kinds of diving apparatus, the valve cannot be completely closed.

These oxygen pressures, however, are never attained in caisson practice as, with compressed air, it would require 4 atmospheres excess pressure for the oxygen tension to be equal to 1 atmosphere, or 15 lbs. Moreover, exposure for some time is necessary before symptoms are produced. While, in deep-sea diving, divers may undoubtedly be exposed to a tension of oxygen which might exert a poisonous effect, or cause severe lung irritation if exposure were unduly prolonged, care is taken under such conditions to make the exposure short.

Bornstein reports that in a fire which took place during the construction of tunnels under the River Elbe, it was necessary to use smoke-helmets, in which the wearers breathed pure oxygen, in order to effect rescue work. As the excess pressure in the tunnels at the time was 2 atmospheres, it is evident that the wearers of the smoke-helmets breathed oxygen having an absolute pressure of 3 atmospheres. Pulmonary irritation was not observed in those who were exposed to this high oxygen tension for thirty minutes. Bornstein, however, justly concludes that this is due to the short exposure, and that this time should not be exceeded.

In the salvaging operations of the submarine F–4, a diver, W. F. L., became entangled and remained for a total time of three hours and forty-five minutes below the surface, at an average depth of 250 feet. The high partial pressure of oxygen to which this diver was subjected resulted in bronchopneumonia, which, according to French, was some time in clearing up.

Description of Compressed Air Illness.—It was not long after compressed air began to be used in construction work and diving before it began to be noticed that exposure to increased air-pressure brought with it a train of symptoms, which varied greatly in severity, from itching of the skin and slight pains in the bones and joints to severe symptoms, such as heart-failure accompanied by paralysis of the extremities resulting often in permanent invalidism, or rapidly causing death. The first account of symptoms arising in workers, due to compressed air, was given in 1841 by Pol and Wattelle.

The types of symptoms they reported may be summed up as follows: difficult respiration; acceleration and hardening of the pulse; muscular pains, often very severe; cerebral symptoms; hebetude; loss of consciousness; deafness and blindness, very often permanent; and sudden death.

The following important conclusions were drawn by Pol and Wattelle from their observations: The compression of air up to 4½ atmospheres is not of itself to be feared; it is readily borne, and infinitely better borne than a rarefication of the air which is much less marked. It is the return to normal pressure which must be feared; this often brings about severe symptoms and may cause sudden death. After exposure to compressed air, the severity of the symptoms observed is proportionate to the pressure originally borne. Young persons support decompression from increased pressure much better than those of middle age. Observations show that the unfortunate effects of decompression are in direct proportion to its rapidity. *There is reason to hope that the most certain and most prompt way of alleviating symptoms would be immediate recompression.*

These opinions of Pol and Wattelle, based upon clinical observations, are entirely correct. Hill remarks that it is strange that these important conclusions should have been neglected by subsequent writers.

Following Pol and Wattelle, LeRoy de Méricourt published the first report concerning the illness of sponge divers. He mentions the frequent occurrence of paralysis and recommends that not less than one minute for every meter of depth should be spent in coming up to the surface, and that each diver should not spend more than two hours and thirty minutes per diem under water.

Symptoms of Compressed Air Illness.—The most recent extensive report on work in compressed air is that of Keays, who describes the symptoms noted in the workers employed in constructing the Hudson River tubes.

Keays makes the following classification of symptoms observed:

1. Cases showing pain in various parts of the body ("bends"), 3,278, or 88.78 per cent.
2. Cases showing pain, with local manifestations, 9, or .26 per cent.
3. Cases showing pain, with prostration, 47, or 1.26 per cent.
4. Cases showing symptoms referable to the central nervous system:
    (*a*) Brain (hemiplegia, or paralysis of one side of the body), 4, or .11 per cent.
    (*b*) Spinal cord:
        (i) Disturbances of sensation, 36
        (ii) Disturbances of movement, 34
        (iii) Combination of sensory and motor disturbances, 10
        Total number of cases, 80 or 2.16 per cent.
5. Cases showing vertigo (staggers), 197, or 5.33 per cent.
6. Cases showing difficult breathing and a sense of tightness in the chest (chokes), 60, or 1.62 per cent.
7. Cases showing partial or complete unconsciousness, with collapse, 17, or .46 per cent.
8. Fatal cases:
    with symptoms belonging to group 3, 6,
    " " " " " 4, 5,
    " " " " " 7, 9,
    Total, 20 cases, or .54 per cent.

From this analysis we are able to judge the wide range of symptoms which may be comprehended under the general title of caisson disease or compressed air illness. In order to give the reader a clear idea of the symptoms arising from exposure to compressed air, the following description of cases is given, typical of symptoms belonging to each of the groups described by Keays.

Cases Showing Pain in Various Parts of Body.—Pains in various parts of the body are known among caisson workers as "bends." After decompression from 2 atmospheres or more excess pressure, fleeting pains in various parts of the body are probably experienced more or less by all caisson workers. The pains are most frequent in the legs, in the neighborhood of the joints. From his observations made during the construction of the tunnel under the River Elbe in Germany, Bornstein gives the following statistics as to the frequency of the location of the pains. In 615 cases of "bends," pains were observed in the lower extremities three hundred and seventy-two times, in the upper extremities one hundred and three times, and in both the lower and upper extremities one hundred and forty times. One peculiarity of the pains is that they occur in the neighborhood of the joints. In the legs, they are usually felt about the knee-joint, and in the arms, about the elbow or shoulder-joint. The pains may be slight and fleeting, or most severe and lasting several days. The pains may be so excruciating as to cause sweating and pallor, and to cause the patient to writhe and cry out with pain. Occasionally local symptoms, such as swelling and collections of air under the skin, may accompany "bends."

Cases Showing Pain, with Local Manifestations.—Pain is more or less general and may be present in the abdomen. Pallor and sweating are present, the patient complains of weakness and dizziness, and may vomit. Keays noted mottling of the body in 13 cases, varying from blotching to bleeding under the skin, the discoloration varying in size from small spots to areas as large as the palm of the hand. In such cases loss of consciousness occasionally takes place.

Cases Showing Pain with Prostration.—In addition to the excruciating local pains, prostration and collapse may be present. The following is a summary of symptoms observed in cases reported by Keays:

1. In 2 cases, there was a semiconscious condition, with marked prostration, cured by recompression.
2. In one instance the man was unconscious and apparently dying, with mottling of the body. Following recompression, the general condition improved, but the man was still very weak. He recovered four days later.
3. One man, while drinking in a saloon, suddenly became unconscious. He regained consciousness when recompressed, but complained of extreme weakness. He recovered two days later, except for weakness in the right arm.
4. One patient was brought to the medical lock unconscious, breathing noisily. He became conscious upon compression. His condition was good; he went home after a few hours' rest.
5. The patient was semiconscious, with marked prostration and mottling of the abdomen. He became conscious and could walk on recompression, but complained of pain in extremities. He recovered at the end of compression.
6. The patient was semiconscious, with marked prostration, difficult breathing, stomach symptoms and mottling of the trunk. He developed heart-murmur. He was improved by 2 compressions but still remained weak. He went home in twenty-four hours. Later he had sharp pains in his left side, and spit blood for several days. He was well at the end of two weeks.

The following case is given somewhat more at length because it shows the efficiency of recompression in an apparently desperate situation.

The patient, twenty-six years old, worked for several months under compression. After working from 7 to 10 a.m. and from 1 to 4 p.m., under 34 lbs. gauge pressure, he went home. Forty-five minutes later he began to have general pain and sickness. When Keays arrived, the man was crying out in pain, was pale, bluish, and sweating. The pulse was rapid and weak. Before the ambulance arrived, the patient became unconscious, with noisy breathing and almost imperceptible pulse. When moved from the bed to the stretcher, he stopped breathing, and for what seemed to be a minute or more he seemed to be dying. After he had received a hypodermic injection of strychnin respirations began again. He was transferred as rapidly as possible to the medical lock, and recompression began, thirty minutes after the onset of symptoms. Massage was given. For some time there was no improvement, but about forty-five minutes later his color was better, and his pulse could be felt. About half an hour later, consciousness was regained, and questions were answered. He could sit up, but felt very weak. He continued to improve during slow decompression. Mottling was marked at one time, but became fainter. Upon the completion of decompression, four hours and thirty minutes later, the patient was wholly conscious, and could sit up with difficulty. The color was good, there was no sweating, the pulse was still rapid and weak, heart and lungs were apparently normal, the abdomen was tender, but not rigid nor distended, mottling was faint, and there was no paralysis. He was discharged from the hospital, cured, four days later.

Keays states that abdominal pain is justly feared by the caisson workers. It was a prominent symptom in many of the severest cases. He states: "With simple abdominal pain, one can never feel sure that a serious case is not threatened."

Mottling of the skin is also a sign of gravity. Itching of the skin, "sand-hog's itch," is a very common symptom on decompression. Hill has ascribed it to small air-bubbles in the subcutaneous fat. Erdman, however, believes that the bubbles are in the sweat-glands, rather than in the fatty tissues, as this itching sensation is quite as common among the leaner as among the plumper workers.

Cases with Symptoms Involving the Nervous System.—Keays reports 4 cases in which symptoms point to embolism by gas-bubbles of the cranial blood-vessels:

1. The first case showed partial loss of power in the left arm and leg. This was relieved by recompression.
2. The next case was one of almost complete paralysis of the right leg and partial paralysis of the right arm, with increased reflexes. It was cured by recompression.
3. One case showed loss of power in the left arm and leg, and was cured by recompression.
4. After working for eight hours at 15 lbs. gauge pressure, this patient was decompressed in two or three minutes. Soon afterward, the right arm and leg became paralyzed, and he could not speak. He was cured by recompression.

Cases Involving the Spinal Cord.—Thirty-six cases showed disturbances in sensation, 9 had numbness or prickling sensation in one leg, 27 had numbness or prickling in both legs, and 17 of these had abdominal pain.

Thirty-four cases showed motor difficulties, classified as follows:

1. One patient had pain in the legs and abdomen, with partial loss of power in the left leg, only relieved by recompression. He recovered in two weeks.
2. Eleven patients had partial loss of power of both legs.
3. One patient had abdominal pain, also cured by recompression.
4. One patient had partial paralysis of one leg, and complete paralysis of the other. He was cured by recompression.
5. One patient had pain in the abdomen and limbs, partial paralysis of both legs, prostration, blotches on the chest and abdomen. He recovered on the third day.
6. Four patients had partial loss of power in both legs, with retention of urine. One of these patients, two years later, still walked stiffly and unsteadily, and was obliged to use a catheter.
7. Seven patients had complete loss of power in both legs, and were cured by recompression.
8. One patient had complete paralysis of both legs, with retention of urine. He finally regained the use of his legs, so that he could walk with difficulty.
9. One case was that of a "green hand" who was given a trial

compression at 33 lbs. for one hour. He was decompressed in sixteen minutes. Paralysis of both legs followed fifteen minutes later. He improved under recompression and could walk. After this, the paralysis returned, with loss of control over the bladder and bowels. Eighteen months later he could walk, but with a spastic gait.

10. One patient had partial paralysis of both legs, with loss of control over the bladder and rectum. He was in the hospital for two weeks, but died later from some unknown cause.

11. In 5 cases, paralysis of both legs occurred, and there was no improvement on recompression. One resulted in death.

Cases Involving Combined Sensation and Movement.—Keays summarizes these cases as follows:

1. In 3 cases there was numbness combined with partial loss of power of both legs. This was cured by recompression.

2. There was one case of numbness and partial loss of power in both legs. The symptoms came back the next day in one leg, and were unrelieved by further recompression.

3. One patient had numbness and loss of power in one leg, complete loss of sensation and of power in the other. He was cured by recompression.

4. In one case there was loss of power in one leg, which was relieved by recompression. Later the patient complained of a dead feeling in both legs, and pain in the abdomen. The symptoms were cured by second recompression.

5. Two patients had complete loss of sensation and power in both legs, cured by recompression.

Cases Showing Vertigo.—Keays reports 113 cases with vertigo only, 42 with vertigo and vomiting, 29 with vertigo and pain in the limbs, 4 with vertigo and abdominal pain, 6 with vertigo and difficult respiration, one with vertigo, pain in the chest, and numbness in one leg, 2 with vertigo, prostration, and mottling.

Snell was the first to call attention to vertigo as a result of compression, in connection with the construction of the Blackwell tunnel.

Cases Showing Difficult Breathing ("Chokes").—This condition resembles a severe attack of asthma. Keays states that many, but not all, cases observed by him occurred when blasting was going on.

Cases Showing Partial or Complete Unconsciousness and Collapse.—The following case, reported by French in connection with the salvaging operations on submarine F-4, illustrates this type of compressed air illness. It was on the occasion of these salvaging operations that the maximum depth ever attained by divers was reached. The depth of water in this instance was from 288 to 306 feet. Divers descended with all possible speed, and remained only the shortest practicable time at the bottom.

In this instance, the diver, W. F. L., entered the water at 10:39 a.m., and reached the bottom at 11:12. He spent fifteen minutes at 90 feet, adjusting apparatus, etc. On commencing to ascend, at 11:24 (12 minutes' stay on the bottom), he found himself foul at 250 feet. He went down again to clear himself, but was unsuccessful. He began to ascend again at 11:35 a.m., and remained at a depth of 250 feet. Diver C. was then sent down. L. was cleared and brought up to 100 feet at 2:25 p.m., the time under water up to this point being three hours and forty-six minutes. Instead of remaining at 100 feet to undergo decompression, L., in spite of telephone instructions to the contrary, climbed up the ladder of his own accord, to a depth of 60 feet, which he reached twenty minutes later. Twenty minutes later, having reached 40 feet, he collapsed, and failed to answer the telephone. He was brought to the surface at once, his diving suit being cut from him. At that time he was conscious, and able to talk, but collapsed a moment later. He was placed at once in a recompression chamber, and the pressure raised to 75 lbs. The patient was unconscious, cyanotic, not breathing, his pulse was imperceptible. Respiration started as the pressure was applied in the recompression chamber. When the pressure reached 75 lbs. the patient suddenly recovered. At 3:14 he was breathing, sitting up, and rational. The pressure was then gradually reduced in the recompression chamber, until 20 lbs. was reached, when he suffered from severe pains in the joints, followed soon afterward by abdominal pains and vomiting. The pressure was increased, and the vomiting left him, the only symptoms remaining being the joint pains, which were exceedingly severe, causing him to kick and scream. Pressure was then slowly reduced, whereupon the patient was removed from the chamber and taken to the sick bay. There were no symptoms showing involvement of the nervous centers. The patient complained bitterly of joint pains. Large areas of subcutaneous hemorrhages appeared over the chest and abdomen. The body was cold and the pulse not palpable at the wrist. Pain was so severe as to require morphin for its relief. The patient gradually improved, though suffering from bronchopneumonia because of the exposure to the high oxygen pressure.

Fatal Cases.—There were 20 fatal cases noted by Keays during the Hudson River tunnel work. In the great majority of these cases, symptoms came on in from fifteen to thirty minutes after decompression. In one instance they came on immediately after decompression; in one instance ten minutes after decompression; in one instance one hour after decompression; in one instance one and a half hours after decompression; and in one instance two hours after decompression.

The general symptoms were pains, often abdominal, with sickness, followed by sudden unconsciousness and collapse. Death followed.

In 4 cases death followed in one hour or less; in 3 cases in five hours or less; in 6 cases in twenty-four hours or less; and in 7 cases death was more or less delayed—from fifty hours to one hundred and forty-four days.

From the foregoing account of the symptoms, it is plain that compressed air illness is a protean malady which may attack the victim in many ways. It is indeed a striking and dramatic affection, coming on as it does without warning when the victim is in the full tide of his powers and feels perfectly well.

True Cause of Compressed Air Illness.—In the past many speculative theories which ignored the operation of physical laws have been put forward to account for compressed air illness. Most of them ascribed the symptoms to the mechanical effects of the increased pressure to which the body was subjected. Little reflection is required to detect their absurdity. It seems indeed remarkable that the fact was lost sight of that the tissues of the body, consisting as they do of a large percentage of water, are, like water, practically incompressible, and instantly transmit pressure in all directions, so that if the pressure on the exterior of the body is equalized by the respiration air at similar pressure, no damage from the pressure can result. Were this not the case, the force exerted by the normal atmospheric pressure would be quite sufficient to render life impossible. The fact (pointed out by Regnard) that the abysses of the sea are teeming with life at depths at which the weight of the column of water is equivalent to a pressure of some 200 atmospheres, or 3,000 lbs. to the square inch, evidently escaped the notice of these theorists.

We now know that symptoms of compressed air illness are brought about, on return to normal pressure, by the liberation of bubbles of gas dissolved under excess pressure in various parts of the body.

By the operation of Dalton's law, the fluids and tissues of the body take up gas in proportion to the partial pressure of these gases in the atmosphere. It is evident that if these gases are absorbed at a given tension and if the individual is subsequently exposed to an atmosphere in which the tension of these gases is very much reduced, the excess of the gases dissolved in the tissues will be given off until their tension is equal to the diminished tension of the new barometric pressure.

If the change from a higher to a lower barometric pressure is made gradually, no harm will result, as the escape of the gases will be gradual also. If, however, the pressure is too rapidly diminished, the difference in tension between the tissue gases and that of the atmosphere becomes so great that the gases dissolved in the tissues of the body are suddenly liberated, with resulting bubble formation.

We have here a fact which perfectly explains not only the symptoms of caisson disease, but their diversity. As different parts of the body saturate and desaturate at varying rates, the tension of the gases may be higher in some parts of the body than in others at any given moment during decompression. This determines the location of bubble formation. If, for instance, the gas-bubbles are liberated in the neighborhood of joints, severe pain is the result, which may be due partly to the plugging by bubbles of the blood supply of the nerves supplying those joints, and partly to the mechanical pressure of the bubbles. If the gases are liberated so suddenly as to fill the capillaries of the lungs full of air-bubbles, the pulmonary circulation becomes at once greatly impeded, if not impossible, and sudden death with respiratory symptoms and cardiac failure or severe collapse may follow. In a similar fashion, the sudden liberation of bubbles in areas of the brain and spinal cord is an effective cause of the form of compressed air illness known as "diver's paralysis" or of cases showing symptoms of involvement of the brain, such as vertigo, apoplectiform seizures, or paralyses of various kinds.

Factors Predisposing to Compressed Air Illness.—In the multitude of observations which have been made on the occurrence of compressed air illness, both in men and animals, certain facts stand forth prominently. (1) *Question of Relative Immunity.*—From the very nature of the circumstances causing compressed air illness, *i. e.*, the liberation of bubbles of gas in some part of the body, there can be no such thing as immunity from compressed air illness, yet it has been observed that while many become victims of this affection, under precisely similar circumstances, others escape, or individuals escape symptoms during weeks and months of work only to be severely affected under what are apparently precisely similar conditions.

Generally speaking, however, we can predict on the basis of physical inspection of the worker whether or not he is likely to have severe symptoms. There seem to be three factors which preëminently influence predisposition to the disease. These are *age, degree of fatness,* and *size.*

To render the worker relatively immune to caisson disease, two physical attributes seem to be required, (1) good circulation, (2) absence of much bodily fat.

The ideal caisson worker would be a young, rather wiry man, with firm, hard muscles, and active movements. It is easy to see how such physical attributes serve to protect their possessor from the onset of symptoms. Because of the lean, firm structure of the body tissues, there is but little fat to dissolve large quantities of excess nitrogen. Desaturation of the different parts of the body will therefore proceed at a much more nearly uniform rate, there being less lag in the process. Furthermore, because of the rapid circulation and high effective weight of the blood as compared to the total weight of the body, saturation, it is true, will take place at a greater rate, but so will desaturation.

In addition to the age and bodily fatness, we may also speak of mere body weight itself as having an influence upon susceptibility to compressed air illness, large individuals being more susceptible than small. This arises from the following physical conditions: Saturation and desaturation are effected by means of a surface (the walls of the air-cells in the lungs). Inasmuch as surfaces are to each other as the squares, and solids as the cubes, of their respective dimensions, it is evident that in small individuals the surface of the lungs will be greater in proportion to the bulk of the body than in large individuals of similar proportions. Therefore saturation and desaturation will proceed at a faster rate in small persons than in large.

This is well brought out in the experimental work which has been done on compressed air illness. Thus the evidence that mice can stand rapid decompression better than rats is reasonably strong, and in general, throughout all the lists of experiments made by numerous investigators, small animals usually stood without harm sudden decompression from pressures which would infallibly kill large animals, such as men.

(2) *Diet.*—It seems probable that the diet of the worker may play some part in his susceptibility to symptoms on decompression. When the diet consists of an abundance of fatty substances, the chyle as it flows from the intestines, and the contents of the lacteals, will contain fat in abundance. This would naturally increase the capacity for absorption of nitrogen, owing to the high solubility of nitrogen in fats. On *a priori* grounds, the best diet for caisson workers would be one consisting more especially of proteins and carbohydrates, with a restricted consumption of fats. Those engaged in compressed air work, especially at high pressures, should indulge sparingly in fried foods, pork, bacon, and the like.

(3) *Influence of Alcohol.*—The multiplied experience of many observers shows that alcoholics have increased susceptibility to caisson disease. There are several reasons for this: (1) In chronic alcoholics the circulation is likely to be impaired, thus retarding desaturation of the slow parts of the body; (2) many alcoholics suffer from an increase of fat in the liver, which serves as a storehouse for excess nitrogen; (3) there is a tendency toward the accumulation of superfluous fats in other parts of the bodies of alcoholics, especially of beer drinkers; (4) it is well known that in heat spells in our large cities, alcoholics are peculiarly liable to heat strokes and heat exhaustion. The hot, humid conditions under which caisson work is often necessarily conducted places the alcoholic under a physiological strain, which he can only meet with difficulty, and at the expense of his circulatory system. For this reason, the circulation is likely to suffer, desaturation be effected with corresponding slowness, and symptoms develop, when those of temperate habits would escape.

(4) *Effects of Local Chilling and Constrained Posture.*—Whenever, by reason of his work, it is necessary for a compressed air worker to maintain a relatively immobile condition, or when an extremity is immersed in cold water, local symptoms, such as bends, are apt to arise on decompression. Bornstein observes that, in many instances in which workers who had hitherto escaped suffered from bends in an extremity,

it was usually found that the affected limb had either been subjected to a prolonged soaking, or that the necessities of the work had caused the subject to assume a strained posture in which the limb was more or less immobile. Such conditions have the effect of slowing the circulation in the affected part. As a shift usually lasts long enough to effect a high degree of saturation, this slowing of the circulation causes slow desaturation in the affected part of the body, and hence favors the occurrence of local symptoms.

So far as divers are concerned, local chilling may be a factor of some importance in the onset of symptoms. The wrist-bands of the diving suit constrict the wrists and may lead to considerable retardation of the circulation in the hand. The water in which the diver works is often very cold, so that on long exposures to moderate depths the diver may become thoroughly chilled before coming to the surface. Such chilling retards the circulation in outlying portions of the body, and symptoms may make their appearance after exposures to pressures which under more favorable conditions would have produced no unpleasant results.

(5) *Factors in the Working Environment.*—Most caissons are hot and humid places to work in. Air while being compressed becomes greatly heated, and the relative humidity is increased in proportion to the increased pressure.* The following table shows the rise in temperature for each increase in pressure:

Pressure Above Atmospheric. Pounds	*Temperature of Air. (F.) Degrees*
0	60.0
14.7	175.8
29.4	255.1
44.1	317.4
58.8	369.4
73.5	414.5
88.2	454.3
102.9	490.6
117.6	523.7
132.3	554.0
205.8	681.0
379.3	781.0

These figures relate to dry air. Moisture in the air will increase these figures, because the specific heat and conductivity of air is raised by moisture.

When the heated compressed air strikes the watery soil in the caisson, the cooling effect may cause precipitation of the moisture in the form of mist. Hill observed such a mist in the Blackwell tunnel, in the course of his visit there in 1911.

Such hot and humid atmospheres have the effect (1) of diminishing the ability of the workers to work, (2) of interfering markedly with the escape of heat from the body. It is well known that physical exertion raises the temperature of the body, and that the body's excess heat must escape; otherwise death, with symptoms of heat stroke, will rapidly ensue. Researches by Rübner, by Flügge, and his co-workers, by Haldane, and by Hill, have shown that the important thermometer measurement, so far as bodily comfort is concerned, is the reading of the wet bulb thermometer. Haldane showed that physical work without dangerous rise in the temperature of the body is an impossibility after the wet bulb thermometer exceeds 84° F. (28.8° C.). The wet bulb temperature of caissons must very often be close to the limit named by Haldane. It should also be borne in mind that wet bulb temperatures in excess of 74° F. produce extreme discomfort, and exhaustion when severe physical toil is attempted, even though the resting subject may be fairly comfortable. As the work required of the "sand hog" is often hard, he must rely on the evaporation of sweat from his body to maintain his bodily temperature within safe limits. We have seen that the compression of air raises the percentage of relative humidity. Moreover, the very density of the air itself renders evaporation more difficult. The absence of through drafts in caissons renders the air more or less stagnant.

---

* Air 40 per cent. saturated at 1 atmosphere will be 80 per cent. saturated at 2 atmospheres, where the temperature is kept constant.

It is no wonder that under such circumstances caisson workers at the end of the shift are bathed in sweat, the pulse is small and frequent, and a sensation of great exhaustion is present. All such conditions must have a marked influence in diminishing the volume of the circulation and hence the rate of desaturation.

During the construction of the Forth bridge, Hunter noted that the most dangerous times, so far as the onset of symptoms was concerned, were (1) when soft wet silt was being removed, and (2) when concrete was being laid. Hill suggests that the excessive sick rate observed under these conditions was due to the increased moisture in the air.

Measures should be taken to prevent the wet bulb thermometer from rising too high in the interior of caissons, and for cooling and drying the air. Hill suggests that the air might be led over tubes of calcium chlorid, a relatively cheap material, which would rapidly absorb the moisture out of the air. The calcium chlorid could then be dried and used again. Electric fans to stir up the air would also greatly assist the evaporation of sweat from the body.

PREVENTION OF COMPRESSED AIR ILLNESS.—Because of the imperfect understanding in the past of the causation of compressed air illness, large numbers of lives have been sacrificed, and still larger numbers of individuals rendered hopeless invalids.

In a list of fatalities in compressed air work, compiled by Heller, Mager, and Von Schroetter, in 1900 there is a list of 97 fatal cases.

While it seems improbable that minor cases of "bends" under high air pressure can be totally eliminated, still it should be possible, by paying due attention to the following principles, to prevent the occurrence of cases of serious illness and death:

1. Careful selection of the personnel.
2. Proper management of decompression.
3. Proper medical supervision of the personnel.
4. Provision for rapid recompression in case of illness.
5. General hygienic precautions with respect to the work itself.

Careful Selection of the Personnel.—Careful medical examination of compressed air workers before assigning them to duty is a prerequisite. The physical attributes which best fit a man to withstand decompression after exposure to high air pressure should be borne in mind. As previously stated, the ideal "sand hog" is a young, lean, wiry individual, free from functional or organic diseases of the lungs and circulatory system. In general, a man of forty-five years of age or more should not be employed. Age, however, is a relative rather than an absolute disqualification. A small wiry man forty-five years of age, presenting no signs of hardening of the arteries, with low blood-pressure, would probably be a better subject than a stout young man of indolent disposition.

As a general rule, the following classes of persons should not be allowed to work in compressed air.

1. Very stout persons.
2. Persons having organic disease of the heart.
3. Persons having organic disease of the kidneys.
4. Persons having respiratory disease, tuberculosis, chronic bronchitis, emphysema of the lungs.
5. Persons showing general disease of the vascular system, such as arteriosclerosis.
6. Persons suffering from chronic catarrh of the nose and middle ear.

Standards of size and fatness must however be regarded as relative. For instance, a person who might be considered somewhat too stout for compressed air work might still have such an active circulation as to enable him to desaturate safely.

The reasons for rejecting persons suffering from organic disease of the lungs, heart, or kidneys are evident. Owing to the effects of these diseases on the circulation, we may expect persons suffering from them to become greatly exhausted by the work.

Management of Decompression.—The proper management of decompression is the fundamental means of avoiding serious cases of compressed air illness. So far as compression or locking in is concerned, the only precaution which it is necessary to observe is that the passages of communication between the middle ear and the outside air, and also those leading to various cells in the bones of the skull, are free, so that any air in the interior of these cavities quickly acquires the new pressure. As previously remarked, these passages are opened up by frequent swallowing or by shutting the mouth, holding the nose firmly with the fingers, and making strong expiratory efforts.

Persons habituated to compressed air can take high pressures with great rapidity. Thus in the diving and slavaging operation of the F-4, diver F. C. descended 306 feet in nine minutes, subjecting himself to an excess pressure of nearly 10 atmospheres, or 150 lbs. to the square inch. In the experimental diving performed in connection with the work of the Admiralty Committee on Deep Diving, Mr. Catto descended 180 feet (6 atmospheres excess pressure) in 1 minute 30 seconds and Lt. Damant in 1 minute 40 seconds.

There is no need, therefore, for the subjection of workers to a gradually increasing pressure, as was advocated by former writers who took a mechanical view of the symptoms brought about by exposure to increased barometric pressure.

The time and method of decompression, however, are of great importance. It is by attention to the management of this all-important period that the toll of suffering and death exacted by compressed air work may be minimized.

(1) *Supersaturation of Body Tissues and Fluids.*—Were it not for the fact that the body tissues are susceptible to a considerable degree of supersaturation with gases before bubbles are given off, symptoms due to bubble formation on decompression would be far more easily

produced. Furthermore, the albuminous nature of the body fluids and their greater viscosity, as compared with water, for instance, discourages the formation of bubbles.

After a careful consideration of all the fatal cases which have been recorded, Haldane found that it was doubtful whether any serious symptoms would ever occur unless the excess pressure exceeded 1.25 atmospheres. At pressures above 1.25 atmospheres, mild cases of compressed air illness began to be recorded, their frequency and severity increasing rapidly with higher pressures unless the time of exposure were shortened or the time of decompression increased. The lowest pressure at which Haldane found records of fatal cases of compressed air illness was 23 lbs., or 1.6 atmospheres of excess pressure. From this Haldane concludes that the blood and tissues of the body will stand supersaturation to 1¼ atmospheres excess pressure without involving the risk of bubble formation.

This conclusion of Haldane enables us to outline the theoretical principles along which decompression should proceed.

It is evident that what is required is, first, to produce as rapid desaturation as possible, and, second, so to manage desaturation that the difference in pressure between the body gases and those of the outside air shall never become dangerous, *i. e.*, ever exceed the ratio of 2 to 1. It is evident that there should be as great a difference as is safe between the tension of the tissues in the body and those of the air breathed, in order to assist the rapid diffusion of gases brought by the blood from the tissues to the lungs. On the other hand, this pressure difference must not become too great, otherwise bubble formation will take place.

No particular precautions are required in decompression from excess pressure not exceeding 18½ lbs. to the square inch, as supersaturation of the body tissues and fluids will prevent bubble formation. It is with the higher pressures, therefore, that we concern ourselves in the following discussion.

(2) *Methods of Decompression.*—Two principal methods of decompression have been advocated: first, gradual decompression, and second, the stage method of decompression.

(*a*) *Gradual Decompression.*—In the gradual method of decompression, the pressure is slowly and uniformly reduced, at a predetermined rate, until atmospheric pressure is reached. In stage decompression, the pressure is abruptly reduced by stages to various levels, a pause being made after each successive reduction, until atmospheric pressure is reached.

In the past, in most of the principal engineering works constructed by compressed air, the uniform method of decompression has been used. Great variations in the period of decompression have been observed. Naturally, in default of knowledge as to the causation of compressed air illness and the relation between the pressure to which the person has been subjected and the severity of the symptoms, the tendency has been to hasten the period of decompression. Air-locks are likely to be small and greatly crowded at the end of shifts. The workers are wet with perspiration from labor in hot and humid caissons. As the pressure is lowered in the lock, the air becomes chilled, and its moisture often precipitated as mist, because of the sudden lowering of its temperature. Just beyond the door of the air-lock lies the prospect of food, warmth, dryness, rest, and recreation. It is no wander then that in the absence of rigid regulations, air-valves are surreptitiously opened to let the pressure out as rapidly as possible. The following have been the times of decompression in some of the well-known works:

TABLE 1. TIMES OF DECOMPRESSION IN SOME WELL-KNOWN CAISSON WORKS.*
* Prepared from table given by Hill.

Date.	Place.	Maximal Pressure (Gauge).	Period of Decompression.
1839	Douchy mines, shaft-sinking.........	2.5 atm.	30 min.
1862	Bayonne, bridge over Adour.........	3.5 atm.	12 min.
1883	Cubsac bridge.....................	7.6 atm.	3.81 min.
1885	Bridge over Eider..................	2.6 atm.	2 min. 5.30 sec.
1889	Wyoming.........................	40.42 lbs.	10 min.
1895	Nussdorf Works, Danube............	2.5 atm.	35 min.
1905	Westcligke Viaduct, Amsterdam......	2 atm.	32½ min.

Gradual decompression is the method which is prescribed in the Dutch law regulating work in compressed air, in the French regulations, and in the laws of New York and New Jersey.

Paul Bert came to the conclusion, as the result of his experiments on dogs, that a decompression period of twelve minutes to the atmosphere was sufficient to avert dangerous symptoms in these animals.

Gradual decompression is the method which has been advocated by Heller, Mager, and Von Schroetter, as the result of their observations in connection with the construction of the locks on the Danube, at Vienna, which furnished them the clinical material for their work on compressed air illness. In order to be safe, according to Von Schroetter, at least two minutes should be used in reducing the pressure 1/10 atmosphere, or for each 1½ lbs. This would lead to the following decompression periods:

20 minutes from 15 lbs.
27 " " 20 "
33 " " 25 "
40 " " 30 "
50 " " 35 "
58 " " 40 "

Decompression at this rate, especially from high pressure, has not been successful in preventing severe symptoms, and even death. This method of gradual decompression has been subjected to the following analysis by Haldane:

"In order to avoid the risk of bubbles being formed on decompression, it has hitherto been recommended that decompression should be slow and at as nearly a uniform rate throughout as possible. We must therefore carefully consider the process of desaturation of the body during slow and uniform decompression. For convenience in calculation, we may imagine the process as occurring in a series of time-intervals, the first half of each of which is spent at the pressure existing at the beginning of the interval, and the second half at the pressure existing at the end. Let us suppose, for instance, that the body has been completely saturated with nitrogen at an excess pressure of five atmospheres of air, and that decompression occurs at a rate of one atmosphere in twenty minutes. The process may be divided into five periods of twenty minutes, during each of which the pressure falls one atmosphere. We can then easily calculate how far desaturation will have gone at the end of each period, and from these data construct a desaturation curve.

"Let us first consider the mean desaturation rate of the whole body, assuming that, when the pressure is suddenly raised or diminished to a certain level, the tissues will on an average saturate or desaturate themselves by 50 per cent. in twenty-three minutes, which was shown above to be a probable average rate. A reference to the curve shows that ten minutes' exposure to the reduced pressure of four atmospheres in excess will reduce the saturation by twenty-eight per cent. of the difference between five and four atmospheres, *i. e.*, by 0.28 of an atmosphere. Hence at the end of twenty minutes the tissues will, on an average, be saturated by 4.72 atmospheres. Ten more minutes at 4 atmospheres will reduce the saturation to 4.5 atmospheres, and ten minutes at three atmospheres will further reduce it by twenty-eight per cent. of 4.5—3, *i. e.*, by 0.42 atmosphere. Hence at the end of the second twenty minutes the saturation of the tissues will be at 4.08 atmospheres. Continuing this calculation, we get the desaturation curve shown in Chart 2, from which it will be seen that when atmospheric pressure is reached, the tissues are still saturated to an excess pressure corresponding to 1.4 atmospheres of air.

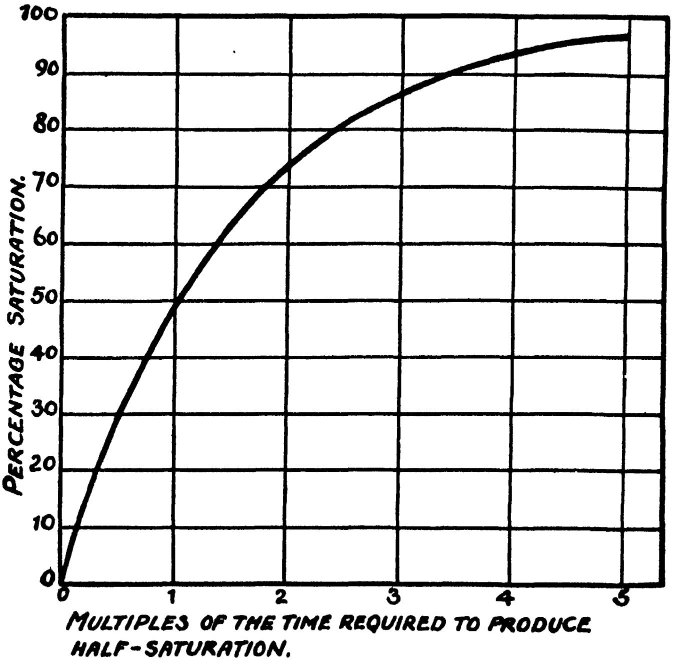


CHART 1 (according to Haldane).—Assuming a part becomes ½ saturated in 23 minutes, it will be 75 per cent. saturated in 46 minutes, 87½ per cent. saturated in 69 minutes, 93.75 per cent. saturated in 92 minutes, etc.

"Inspection of Chart 2 shows that with uniform decompression the nitrogen pressure in the body lags behind that of the air, and that (in the case of the slowly desaturating parts) the amount of the lag increases during the whole time of a decompression lasting 100 minutes. No other result seems possible, and actual experiments point strongly in the same direction, as will be shown presently. We must emphatically dissent from the conclusion drawn by Heller, Mager, and Von Schroetter that decompression at the uniform rate of twenty minutes an atmosphere prevents any dangerous retention of gas in the body. To prevent a maximum lag of more than one atmosphere, it would be necessary to decompress at a rate of over one and a half hours an atmosphere if the decompression were uniform and from an excess pressure of 5 atmospheres.*

"The examples given will be sufficient to illustrate the extreme slowness at which desaturation must occur with a uniform rate of decompression. This slowness has never hitherto been recognized, but must evidently be reckoned with in devising measures for the prevention of caisson disease."

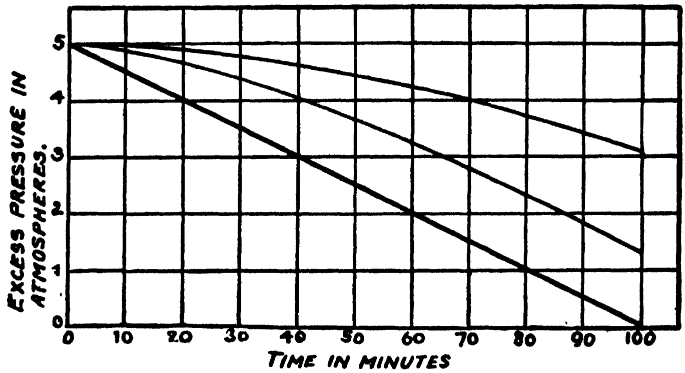


CHART 2 (according to Haldane).—SHOWING THE LAG IN DESATURATION OF QUICKLY AND SLOWLY SATURATING PARTS OF THE BODY WITH UNIFORM DECOMPRESSION.

This criticism of Haldane's on the dangerous lag in desaturation peculiar to slow decompression seems unanswerable. In justice to the recommendations of Heller, Mager, and Von Schroetter, however, it should be stated that, at the time of their studies, although they realized that, because of lack of uniformity in the distribution of the blood, some portions of the body would saturate and hence desaturate more slowly than others, the fact (discovered by Vernon) that nitrogen gas was approximately 6 times more soluble in fats, oils, and fat-like bodies (such as for instance lipoids of the nervous system) than in the other tissues was unknown.

The dangerous lag in desaturation shown by Haldane's analysis is more especially due to the excessive solubility of the excess nitrogen in the fats and oils. The excess pressure of 1.4 atmospheres (21 lbs.) remaining in the quickly saturated parts of the body, after gradual decompression from 5 atmospheres in one hundred minutes, as shown by

---

[*] "It is evidently a mistake to assume that a given rate of uniform decompression, such as twenty minutes per atmosphere, is either necessary for safety in all cases, or would be actually safe except from some limit of pressure. From a pressure below this limit, the rate will be unnecessarily slow, and from above it dangerously fast."

Haldane's calculations, is not after all excessive and is probably within the supersaturation limits, without bubble formation, of the more quickly saturating parts of the body. It is the excess pressure of 3.4 atmospheres in the slowly saturating parts which, as Haldane puts it, constitutes a formidable excess. It is precisely in these slow parts, among which portions of the nervous system must be included, that bubble formation is likely to be followed by severe symptoms. These considerations led Haldane to work out his theory and practice of stage decompression.

(*b*) *Stage Decompression.*—As previously mentioned, Haldane, as the result of inquiry, found that injurious symptoms practically never occur on decompression, unless the excess pressure exceeds 1.6 atmospheres (2.6 atmospheres absolute, 23 lbs. gauge pressure, or a ratio of 2.6 to 1), although slight symptoms may occur as a result of rapid decompression from such a pressure. Inasmuch as the relative volumes of a gas at different pressures are as the ratio of these pressures to each other, it seems likely that it would be safe to decompress rapidly from any excess pressure to a lower pressure, provided the ratio of change in absolute pressure is not greater than the 2.6 to 1 just mentioned.

Haldane considers that, although the absolute pressure may be reduced by somewhat more than ½, to be on the safe side in actual practice, the ratio of reduction should be as 2 to 1. By making this reduction the first step in decompression, Haldane states that the following advantages are obtained:

> "The process of desaturation can therefore be hastened very greatly, by rapidly reducing the absolute pressure to ½, and so arranging the rest of the decompression that the saturation in no part of the body shall ever be allowed to increase more than about double the air pressure. The main advantage of this plan is that the discharge of nitrogen from the tissues is from the outset of decompression increased to the greatest rate which is safe. The rate of discharge evidently depends on the difference in the partial pressure of nitrogen in the venous blood and in the alveolar air; and by keeping this difference at the maximum consistent with safety, a great saving in time is effected."

Haldane has called this method stage decompression, and his general principles consist first in dropping the pressure rapidly until ½ the absolute is reached, and, from this point on, decompressing slowly at a calculated rate until atmospheric pressure is reached.

The following is an illustration of the application of this method in a practical instance (quoted from an article by Boycott, Damant, and Haldane *):

> "It will be convenient to consider first the case of diving to a very great depth, and we shall take as an extreme example the case of exposure at a depth of 35½ fathoms (213 feet) of sea-water, corresponding to an excess pressure of nearly 6.5 atmospheres, or an absolute pressure of 7.5 atmospheres.
>
> "Let us first suppose that the body of a diver is completely saturated with the nitrogen of air at this pressure, and that it is required to conduct his ascent to surface as rapidly as possible but without any risk of symptoms due to bubble formation, *i. e.*, in such a way that, in accordance with the principles already laid down, the nitrogen pressure in no part of the body shall ever be more than double that of the air breathed at the same time.
>
> "The first step would obviously be to reduce the absolute pressure to about half, *i. e.*, from 7.5 atmospheres absolute to 3.75 or from 6.5 atmospheres in excess to 2.72. This would be *ex hypothesi* the greatest initial drop in pressure which would be perfectly safe. The remainder of the decompression would evidently need to be conducted in such a way that the maximum partial pressure of nitrogen in any part of the body should diminish at double the rate of the fall in absolute pressure of the air. The ascent of a diver can be conveniently regulated from the surface by signalling to him to stop or come on at every ten feet as indicated on the pressure gauge attached to the pump. We may therefore divide the ascent into stages

---

* "Prevention of Compressed Air Illness." Cambridge Journal of Hygiene, 1908, viii, 359.

> of ten feet, and the short periods occupied in the actual ascents may be neglected.
>
> "Since the depth was 213 feet, corresponding to 246 feet of water in absolute pressure, it would be safe to come up at once to a depth corresponding to 123 feet of absolute water pressure, *i. e.*, to 90 feet of actual depth. Consequently the first stage would be a rapid ascent of 123 feet, and it would be necessary to wait here before the next ascent of 10 feet, until the maximum partial pressure of nitrogen in the body had fallen to that of the nitrogen in air at 2 x (80 + 33) = 226 feet of absolute water pressure. The difference between 246 and 226 is 20, and this is 16 per cent. of 213 — 90 = 123, the difference between the original and the reduced pressure. The most slowly desaturating parts of the body will, according to our previous calculations, take 75 minutes to give off half of any excess of nitrogen which they may contain at any given air pressure; by inspection of the curve (Chart 2) it will be seen that they will take about nineteen minutes to lose 16 per cent. of the excess. Hence a delay of nineteen minutes would be necessary at 90 feet before coming up to 80 feet. At 80 feet the partial pressure in the body would require to fall an amount corresponding to 20 feet, which is about 17½ per cent. of 193 — 80 = 113, the new difference in relative pressure between the nitrogen in the body and in the air. This would necessitate a delay of twenty-one minutes before ascending to 70 feet. The further delays needed would be twenty-three minutes at 70 feet, twenty-six minutes at 60 feet, thirty minutes at 50 feet, thirty-five minutes at 40 feet, forty-two minutes at 30 feet, fifty one minutes at 20 feet, and sixty-two minutes at 10 feet. It would thus take three hundred and nine minutes, or more than five hours, to reach surface."

This shows the very long time required to effect decompression safely by any method wherever the exposure has lasted a sufficient time to allow thorough saturation of the body tissues to occur.

The times necessary therefore for safe decompression from the higher pressures are so long as to be wholly impracticable, if the exposure is not reduced so that decompression is begun before full saturation of the tissues has taken place.

By adjusting the time of exposure to the pressure, Haldane has worked out a series of decompression times for divers by the stage method just described, which not only renders work in great depths free from serious risks to life, but places the periods of decompression within practical limits.

It should be noted at this point that there is a fundamental difference between diving work and caisson work. The diver usually works for short periods under high pressures, whereas the caisson worker is exposed for much longer periods to more moderate pressures. We thus find that, when divers suffer from compressed air symptoms, these very rarely consist of joint pains, such as "bends," but are far more likely to be serious symptoms of paralysis and collapse. This is due to the fact that, in divers, the very slowly saturating parts such as bones and joints have had, owing to the shortness of the exposure, but little time to proceed far with saturation. Hence, the symptoms arise in the more quickly saturating parts of the body. The longer shift of caisson workers, however, gives opportunity for a greater degree of saturation in the slowly absorbing parts of the body.

(*c*) *Stage Decompression Applied to Caisson and Tunnel Work.*—The method of stage decompression advocated by Haldane and his co-workers for divers has been modified somewhat to meet the special case of caisson and tunnel workers, for whom we must provide decompression from exposures usually lasting not less than three hours to a shift, and not less than six hours each day. With such exposures, the first step, as in the case of divers, is to reduce the initial absolute pressure to one-half. Calculation shows that further decompression by the stage method so closely approximates uniform gradual decompression that the remainder of the "locking out" may be conducted by uniform slow decompression.

The following illustrative example, quoted from Haldane and his colleagues, will serve as an illustration of this method of decompression, as applied to caisson and tunnel workers.*

> Supposing the men were working at an excess pressure of 24 lbs. (an absolute pressure of 24 + 15 = 39 lbs.) in three-hour spells, with an hour's interval for a meal, the first step on locking out, as in the case of divers, would be rapidly to reduce the absolute pressure to one-half $\left(\frac{24 + 15}{2}\right.$ = 19½ lbs., or an excess pressure of 4½ lbs.). After the first three-hour spell of work, the slow decompression would be at the rate of 1 lb. in three minutes, or 3 x 4½ = 13½ minutes in all. After the second shift the rate would be 1 lb. in five minutes, corresponding to 22½ minutes in all. If the men were to stay for the whole period in compressed air, the rate of slow decompression would be 1 lb. in seven minutes, corresponding to 31½ minutes in all.

Table 2, worked out by Haldane and his colleagues, shows the rate of decompression by the stage method, in caisson and tunnel work.

TABLE 2. RATE OF DECOMPRESSION IN CAISSON AND TUNNEL WORK.
(Boycott, Damant and Haldane.)

	Number of minutes for each pound of decompression after the first rapid stage.		
Working pressure in lbs. per sq. inch.	After first three hours' exposure.	After second or third three hours' exposure, following an interval for a meal.	After six hours or more of continuous exposure.
18–20 lbs.	2	3	5
21–24 "	3	5	7
25–29 "	5	7	8
30–34 "	6	7	9
35–39 "	7	8	9
40–45 "	7	8	9

In actual practice the results by the stage method, so far as divers are concerned, have met the indications. By the stage method of decompression, divers were decompressed without serious symptoms in the salvaging operations of the F–4, after being exposed to an excess pressure corresponding to 306 feet of water (nearly 10 atmospheres gauge pressure). The only exception was one diver who became fouled, and remained three hours and forty-five minutes under the water, and who furthermore disregarded instructions in making his ascent. This diver certainly would have died had not means for immediate recompression been at hand.

In caisson and tunnel work, however, and in experiments on animals, decompression by the stage method has not given the results which might be hoped for. Bornstein, as the result of his observations at the Elbe tunnel works, where there was an excess pressure of 2 atmospheres, compared the effect of decompression by stage and by uniform method with results given in Table 3.

From this table it would seem that there is a slight advantage on the side of the stage method, but by no means a decisive one.

Subsequently in the course of these works, the men were obliged to climb a steep staircase immediately upon leaving the air-lock. This exercise after decompression proved far more effective in reducing the number of cases of "bends" than decompression by the stage method.

---

* BOYCOTT, DAMANT AND HALDANE: Prevention of Compressed Air Illness. Cambridge Journal of Hygiene, 1908, viii, 374 *et seq.*

On the other hand, using the method of uniform decompression, Hersent, at Bordeaux, in 1894, after animal experimentation, found 3 workers who were willing to subject themselves to exposure to high air pressures. The men were enclosed in a steel chamber, the experiments being conducted under the observation of a Commission composed of 5 members of the Bordeaux Faculty of Medicine.

In one experiment, the individual was subjected to an excess pressure of 4.8 kilograms to the square centimeter (68.27 lbs. to the square inch). Thirty-five minutes were consumed in reaching this pressure; the length of the exposure was one hour, and the time of decompression two hours and three minutes. The only symptom observed after decompression was a little itching.

Table 3. Comparative Effects of Stage and Uniform Decompression.

Days.	Workers.	Cases of Illness.
20 stage	526	15
16 uniform	528	17
18 stage	529	12
16 uniform	529	14
14 stage	536	12

In the second experiment, a pressure of 5 kilograms to the square centimeter (71.16 lbs. to the square inch) was reached after compression lasting one hundred and fifty minutes, with no unfavorable results except a little itching, as in the first experiment.

On the third trial, the same subject was compressed 5.4 kilograms to the square centimeter (76.81 lbs. to the square inch) in forty-five minutes, remained under the pressure one hour, and was decompressed in three hours and three minutes.

Hersent decompressed men with safety after one hour's exposure in:

26	minutes	from	2.5	atmospheres
46	"	"	3.0	"
60	"	"	3.5	"
77	"	"	4.0	"
100	"	"	4.5	"
150	"	"	5.0	"
183	"	"	5.5	"

Hill points out that Hersent safely used a method which is theoretically the poorest, namely, from 5 to 4 atmospheres in forty-five minutes, from 4 to 3 atmospheres in thirty-five minutes, from 3 to 2 atmospheres in thirty minutes, from 2 to 1 atmospheres in twenty minutes, and from 1 to 0 atmospheres in fifteen minutes, inasmuch as the decompression rate was slower at first and more rapid at the end.

Hill and Greenwood, in their experiments, successfully exposed themselves to high pressure; Hill to 75 lbs. once, and Greenwood to 92 lbs. once and 75 lbs. three times. During the experiment in which Greenwood reached the excess pressure of 92 lbs., fifty-four minutes were spent in reaching this pressure, whereupon the pressure was gradually reduced, two hours and seventeen minutes being required to reach atmospheric pressure. On leaving the chamber, Greenwood noticed some itching in both forearms, especially the right, which was followed by pains in both arms.

Hill and Greenwood came to the conclusion that it was an important matter during decompression to move and turn every muscle and joint of the body, so as to accelerate the circulation. They found such precautions sufficient to remove disagreeable symptoms.

It seems evident, then, that while, from a theoretical standpoint, stage decompression should be far superior to uniform decompression, in practice it is possible to decompress from high pressures with the uniform method with apparent safety.

In his paper delivered before the 15th International Congress on Hygiene and Demography, Japp, who was the Managing Engineer for S. Pierson and Son, the contractors on the four East River tunnels for the Pennsylvania Railroad, suggested that the times allowed for decompression by the stage method for pressures between 35 and 45 lbs. are too long for practical purposes, for, according to Haldane's figures, it would take ninety and one-half minutes to decompress from 40 lbs. pressure. Japp assumes that an excess pressure of 25 lbs. in the tissues would be safe at the close of decompression. He has therefore drawn up a table (Table 4) of procedure in which Haldane's theory of stage decompression is applied, but which permits the maximum excess pressure in the tissues to be 25 lbs. instead of 19 lbs. This has the effect of shortening the times materially.

In the course of the construction of the East River tunnels, Japp relates that it was necessary to raise the pressure in the tunnel to 40 lbs. gauge. This occurred after he had become acquainted with Haldane's theory of stage decompression. Fortunately it was possible to arrange to have the men exposed to this pressure pass through 3 sets of air-locks. The decompression was carried out in the following way: The men were ordered to take five minutes in the first lock, decompressing from 40 lbs. to 29 lbs.; then followed a walk of 1,000 feet in a section of the tunnel which was kept at a pressure of 29 lbs. This required about 10 minutes, including waiting to get into the second air-lock, and collecting stragglers. Eight minutes were spent in the second air-lock, where the pressure went from 29 to 12½ lbs. (27½ lbs. absolute), or one-half the original absolute pressure $\left(\frac{40 \text{ lbs.} + 15 \text{ lbs.}}{2} = 27\tfrac{1}{2} \text{ lbs.}\right)$

Another walk of 1,000 feet in the second tunnel section took place at this pressure, and when the third lock was entered, the pressure was reduced to atmospheric in fifteen minutes. Thus, forty-eight minutes in all were spent in decompressing from 40 lbs. excess pressure, by this method. Japp calculates that, in the course of such decompression, the maximum excess pressure of gas in the body tissues was 27 lbs. Thus the men did what was equivalent to emerging instantaneously from a pressure of 27 lbs. No severe or fatal cases resulted under these conditions. Three hundred and thirty men were employed for thirty-six days, working two shifts of three hours each, separated by a rest interval of three hours at atmospheric pressure. There were over

20,000 individual decompressions without a mishap. If the decompression had been conducted according to the modified table submitted by Japp, the maximum gas in the tissues on emerging would have been 25 lbs. instead of 27.

TABLE 4. DECOMPRESSION PROCEDURE, BASED UPON 25 LBS. MAXIMUM AIR SATURATION OF BODY ON EMERGING.

Gage pressure.	Reduce pressure in 3 minutes to:	Total time in air-lock after 8 hours' work.	Total time in air-lock after 3 hours' work.	Total time in air-lock after 2 hours' work.	Maximum air saturation of body on emerging.
Pounds	*Pounds*	*Minutes*	*Minutes*	*Minutes*	*Pounds*
27	6	9	..	..	25
30	7½	24	..	..	25
32	8½	33	25	..	25
35	10	..	35	..	25
40	12½	..	48	..	25
42	13½	..	51	37	25
45	15	..	..	42	25
50	17½	..	..	48	25

On the other hand, it should be pointed out that while, in this instance, the theoretical maximum saturation of the tissues on emerging was 27 lbs., it was probably below this figure usually, for the reason that the men walked a distance of 2,000 feet, or very nearly half a mile, during the course of decompression.

Moreover, Japp informs us that all the men employed at this stage of the work were seasoned compressed air workers. The previous experience of these men implies that physically they possessed the attributes which make the individual wall adapted to work at high barometric pressure, *i. e.*, they had good circulations and were not encumbered by superfluous fat.

Aids to Rapid Desaturation of the Body.—In addition to so managing decompression after exposure to high barometric pressure that at no time shall there be a dangerous excess of gas stored in the tissues of the body, there are two ways in which we can help the body to get rid of the excess gas which it holds:

1. By increasing the rapidity of the circulation.
2. By breathing a gas (*i. e.*, oxygen) which of itself is harmless so far as storing in the tissues is concerned, but which will displace the excess of nitrogen.

If vigorous exercise is taken during the time of decompression, a greater number of rounds of the circulation will occur in the same period. Consequently the amount of nitrogen gas discharged will be greatly increased.

In air-locks, however, this means is not made use of as a rule. The locks are small and crowded, the men are more or less fatigued from the work of the previous shift, and the tendency is to remain as passive as possible, many men taking naps while the pressure is being reduced. Moreover, the chill caused by the loss of heat in the air as the pressure declines has a tendency to empty the skin of blood, contract the surface vessels, and increase the resistance to the circulation. Besides this, sleep itself retards the circulation. Thus Boycott and Damant found that dormice, weighing only 10 or 12 grams, could usually be killed, when hibernating, by decompressing them in five seconds from 75 lbs. pressure, whereas decompression in the same time from 120 lbs. had hardly any effect on them when they were in a lively condition.

It is evident that we can hasten the process of desaturation after exposure to excess pressure by causing the individual to breathe an atmosphere in which the partial pressure due to nitrogen is zero. This can be done by having him inhale oxygen gas. In this way the greatest possible difference in tension between the nitrogen in the tissues and that of the air breathed is created, the nitrogen being rapidly disengaged. This will take place if an atmosphere of oxygen is breathed, at a tension corresponding to the tension of nitrogen in the tissues. It will, of course, take place with still greater rapidity if the tension of the oxygen is less than that of the nitrogen in the tissues. Unless the difference in tension between the oxygen breathed and that of the nitrogen in the tissues is too great (*i. e.,* greater than 2 to 1), no bubble formation can take place because the nitrogen as it leaves the tissues enters into solution in the blood. Because of the dangers of oxygen-poisoning this method would not be practicable if it were necessary to use tensions of oxygen in excess of 2 atmospheres. The observations of Bornstein show that, provided the period of inhalation is not more than thirty minutes, oxygen at a tension of 2 atmospheres will not produce symptoms.

In work at moderate pressures, the inhalation of oxygen might well be dispensed with, exercise being substituted, if necessary, as a means for assisting the process of desaturation. When, however, it is necessary to decompress from high pressures (35 lbs. and over for caisson workers) the risk of the onset of symptoms could be very materially reduced by commencing the inhalation of oxygen after the first rapid reduction in pressure (in decompression by the stage method). The oxygen would be breathed from a rubber bag, and could be readily and cheaply generated by the use of oxylith.

TREATMENT OF COMPRESSED AIR ILLNESS.—*Recompression.*—Recompression, if immediate, is the most effective means at our command for the treatment of decompression symptoms. As Hill put it, "all measures are as nothing, as compared with the efficacy of recompression, by means of which men have truly been raised from the dead."

The first suggestion as to the value of recompression is found in the report made by Pol and Wattelle, on their work at Douchy, in 1854. It will be remembered that they stated among their conclusions: "There is ground for the hope that recompression will relieve symptoms coming on after decompression." Hoppe also suggests recompression as an efficient method for relieving compressed air illness. Workers themselves have found that relief from the often excruciating pains of "bends" was found by reëntering the caisson. It has also been the custom among the Greek sponge divers to descend below the water if they suffered from symptoms after reaching the surface. Smith, in his report on the caisson work on the Brooklyn Bridge, suggested the use of a recompression chamber.

The first medical air-lock was put into operation by E. W. Moir, at the original Hudson River tunnel works, in 1890, and proved its efficacy. Since then a medical air-lock has been part of the essential equipment of caisson works.

F. W. Keays reports that, in the construction of the East River tunnels, recompression relieved 90 per cent. of the 3,067 cases of pain treated, failing to give relief in only 103 of the cases.

The method of recompression used in the East River tunnel works was to place the patient as soon as practicable in the recompression chamber, and then raise the pressure to the point at which the subject had been working in the tunnel. It was found that while the pains were often relieved by a lower pressure, the results were more likely to be permanent if the full tunnel pressure was employed. As soon as the pressure had reached the full tunnel pressure, decompression was begun, the time of decompression being fully twice as many minutes as there were pounds of pressure.

Keays found that the best results were produced by reducing the pressure rather quickly for the first 10 or 15 lbs., after which point decompression was very slowly effected. If able to do so, the patient was directed to move about during the period of decompression, as it was found that exercise, especially of the affected part, was of assistance in permanent relief.

Occasionally the symptoms returned after the patient had left the lock. In such cases the patient was recompressed a second time. In some instances it took three or four recompressions before permanent relief was secured.

While recompression chambers should always be available in caisson work, they are not always necessary for diving operations. The Admiralty Committee states that even if very serious symptoms have already developed. and the diver is helpless, it is far safer to open his valve, give him plenty of air, and then drop him down slowly and steadily on the life line until he recovers or the bottom is reached. He will probably have recovered by the time he is down a few fathoms. Another diver can then be sent after him shortly. If he has no symptoms as yet, he can go down himself in the ordinary way until a safe depth is reached. In any doubtful case, where it seems possible that symptoms may develop, the diver on coming to the surface might remain in the water or on the diving ladder for ten minutes before coming on board and having his helmet unscrewed. He could thus very easily descend again if he began to feel any symptoms. In coming on board, he should not undress for another twenty minutes.

VENTILATION OF CAISSONS.—(1) *Carbon Dioxid.*—As a rule, sufficient air escapes beneath the lower edges of caissons to prevent any excessive accumulation of carbon dioxid from the lungs of the workers. As long as the tension of the carbon dioxid in the air of the caisson does not rise above 1 or 2 per cent. of an atmosphere, no harmful effects can be produced. It should be borne in mind, however, as previously discussed, that as the pressure is increased the carbon dioxid tension must be correspondingly reduced. If, under a pressure of 2 atmospheres in the caisson, the carbon dioxid should accumulate, because of defective ventilation, to the extent of 1 or 2 per cent., such a percentage would have the same effect as 4 or 8 per cent. of carbon dioxid at atmospheric pressure. This would produce severe panting and exertion, hence not only greatly reducing the efficiency of workers, but throwing such additional strain on the circulation as to render the workers liable to symptoms of compressed air illness on decompression. Such accumulations of carbon dioxid are possible during the operation of concreting caissons, after they have been sunk to their bearings, or when the caisson is being driven through water-tight strata, such as clay. Under such circumstances practically no air can escape from the caissons, and the supply of fresh air to the caisson can be very materially reduced.

As Hill points out, there is no need whatever for the excessive air supplies in caissons which are advocated by Snell, who thought that the accumulation of carbon dioxid had a considerable effect in the causation of decompression symptoms and advocated a great increase in the air supply. As Hill justly observes, the money spent in securing this enormous supply of compressed air could be utilized to far better advantage in cooling and drying the air of caissons and in supplying electric fans to keep the air in circulation.

(2) *Deleterious Gases in Caissons.*—Where work is carried on in compressed air, at considerable pressure, the possibility of the formation of carbon monoxid gas in the cylinders of air compressors merits some attention. Owing to the great heat developed during the compression stroke, in air compressors, oil used for lubricating cylinders may flash and produce carbon monoxid gas, due to the fact that it is incompletely consumed. Attention should therefore be given to the quality of oil utilized to lubricate the cylinders of air compressors for the supplying of compressed air for human consumption. Only oils of very high test should be used for this purpose. Castor oil seems to be one of the best lubricants, so far as air-pumps for the use of divers are concerned. French advocates the use of this oil.

Where rocks are encountered in the process of sinking caissons, or in the driving of tunnel-headings through rocky formations, blasting must often be resorted to. The explosion of dynamite liberates gases which under favorable conditions consist of carbon dioxid, nitrogen, and oxygen. Under unfavorable conditions, as, for instance, when the dynamite is damp, or when for any other reason combustion has been incomplete, the gases given off will also contain carbon monoxid, nitrous oxid, methan, hydrogen, and sulphuretted hydrogen. According to Haldane, the amount of carbon monoxid formed may reach 36 per cent. It is well known that carbon monoxid is a colorless, odorless, highly poisonous gas, its poisonous properties being due to its great affinity to the hemoglobin of the blood, which is some 200 times greater than that of oxygen. In this way, an atmosphere containing 1/10 of 1 per cent. carbon monoxid might be expected to displace 50 per cent. of the oxygen in the blood, thus leading to symptoms of acute oxygen starvation. The presence of the carbon monoxid in the air is imperceptible to the victim, the fact of its presence not being revealed until symptoms of poisoning take place. Loss of consciousness and collapse may follow, after slight feelings of sickness and dizziness. As a rule, the amount of carbon monoxid present after blasting in tunnel-headings constructed by the use of compressed air will not be considerable. As a measure of safety, however, it is well to blow such headings out, after blasting, with air-pipes. The safety of the air may also be tested by exposing small animals, such as mice or canaries, to the air. Because of their high bodily temperature and the great rapidity of their circulation, such small animals are affected by an atmosphere containing carbon monoxid much more rapidly than a man.

DEVICES FOR THE SAFETY AND COMFORT OF WORKERS.—*Gauges.*—Because of the possible onset of symptoms, all air-locks should be provided with gauges, both on the inside and the outside, so that the pressure within the air-lock may be properly controlled. Recording gauges are also advisable, so that the rate of fall of the pressure and the time spent in decompression may be recorded. All air-locks should be under the supervision of a competent and reliable lock tender, who will carry out to the letter the prescribed methods and times for decompression.

Washrooms and Locker Rooms.—In any considerable compressed air works, suitable washrooms, locker rooms, and barracks should be provided for the use of workers. Compressed air workers should be afforded the fullest opportunity to change their working garments, wet with perspiration, for dry ones, and to enjoy the beneficial stimulus of a bath. Spray shower baths should be provided, furnishing water at a considerable pressure, in the form of a fine spray. Such baths combine the stimulating effects of the cold shower with the agreeable and cleansing properties of hot water. As warm water forcibly thrown in the form of a fine spray possesses the stimulating qualities of water at a lower temperature and at the same time the superior cleansing qualities and comfort of a warm bath, the stimulus to the circulation assists in desaturating the body of the remaining nitrogen in the tissues.

At the close of decompression, wherever the pressures exceed 23 lbs. gauge, barracks should be provided, furnished with suitable cots, in which workers may remain for at least an hour after undergoing decompression, for the purpose of observation. The records of physicians in charge of medical supervision of the personnel in large compressed air works are full of instances in which workers left the caisson apparently in good physical condition only to be picked up later, collapsed, on the street or in some neighboring saloon, suffering from severe decompression symptoms.

CONDITIONS DUE TO DIMINISHED BAROMETRIC PRESSURE

In the preceding section, we have considered the effects of increased barometric pressure upon the organism, the morbid consequences of intensive exposure to such pressure, and means of prevention and treatment.

It now becomes necessary to consider the opposite condition, *viz.*, the effects of exposing man to diminished barometric pressure. In the past, man has been exposed to diminished barometric pressure chiefly in inhabiting and exploring the mountainous regions of the earth, and occasionally in balloon ascensions. The present, and the much greater, impending, future development of aërial navigation will multiply the occasions requiring exposure to diminished barometric pressure and make it even the more important that we should fully understand the effects. Nor is the study of the effects of diminished barometric pressure of importance solely from a practical standpoint, but the study of these conditions has already thrown much light upon physiological processes, and is placing us in possession of knowledge which has proven of great utility in other fields of medicine.

It has long been a matter of common knowledge that, whenever certain altitudes are exceeded, a train of symptoms ensue which may vary all the way from slight physical discomfort to grave symptoms, perhaps loss of consciousness and even death. Various names have been ascribed to these effects of high altitude, such as "mountain sickness," "Alpine vertigo," and, in South America, "puña" or "soroche" (antimony). The latter term arose from the fanciful belief that the symptoms were caused by poisonous metallic emanations (mountain sickness being common in the lofty mining regions in Peru). We owe, however, to the classic researches of Paul Bert the discovery that the symptoms caused by exposure to diminished atmospheric pressure are in reality due to the lack of the oxygen pressure to which the body is accustomed. In this classic on barometric pressure, Paul Bert reviews the entire literature of the world for data in regard to mountain sickness, and especially the writings of travelers and explorers. He is able to find specific references to the symptoms caused by high altitudes as early as 1596, in Robert Regnault Cauxois's translation of the journeys in South America from 1534 to 1554 of the Jesuit Acosta. It speaks of a sickness "strange and unwonted" which suddenly attacked him in climbing the mountains of Peru.

Until the invention of the balloon we find references to mountain sickness mainly confined to the writings of explorers who, for the most part, contented themselves with referring to the various symptoms which they experienced without going into any scientific discussion of their cause. However, with the enthusiasm, the increased opportunities for scientific observations, and the competition for altitude records which were brought about by the development of the balloon, and subsequently the invention and development of the aeroplane, an increasing volume of scientific observations has been directed to the study of the effects of diminished barometric pressure. At present this is a field of medical research in which our knowledge is both rich and varied.

Symptoms of Mountain Sickness.—There is a wide variation in different individuals in the altitude at which symptoms of the exposure to diminished barometric pressure begin to make their appearance. For most persons the height of 10,000 feet, corresponding to a barometric pressure of 516 millimeters, forms a critical point above which symptoms begin to make their appearance. On the other hand, in susceptible persons, the symptoms may be severe and make their appearance long before the previously mentioned critical altitude of 10,000 feet is reached, and such persons may be so uncomfortable at relatively low levels (say between six and eight thousand feet) that they are forced to return to lower levels.

One of the most graphic accounts of the onset of mountain sickness by a non-medical writer is that contained in von Tschudi's book,* which is quoted by Paul Bert as follows:

> "I was climbing the mountain vigorously, when I felt the formidable influence of the rarefied air; I felt in walking a strange discomfort. I had to halt in order to breathe, even then I could hardly do so; if I tried to walk an indescribable agony seized me. I heard my heart pounding against my ribs: my breathing was short and gasping; I had an enormous weight on my chest. My lips were blue, swollen and fissured; the conjunctival capillaries broke open and from them welled forth a few drops of blood. The sensations were singularly blunted; sight, hearing and touch were affected; before my eyes floated a thick cloud, grayish and often reddish, and I wept blood-stained tears. I felt myself between life and death; my head spun, my senses failed and I stretched myself trembling upon the ground. In truth, had the greatest riches, or immortal glory awaited me a few hundreds of feet farther up, it would have been both physically and morally impossible for me even to have moved my hand in their direction."

The power of adjustment of many individuals is such that they experience no symptoms until an altitude of some 14,000 feet, corresponding to a pressure of 444 millimeters, is reached, while the exceptionally fit and hardy individual may attain an altitude of 18,000 feet, corresponding to a barometric pressure of 382 millimeters, without much discomfort, before symptoms worthy of note are experienced.

---

* "Peru, Reiseskizzen aus den Jahren 1838–1842." 2 vol., Saint Gallin, 1846.

The advent of mountain sickness is also notably affected by the manner in which the altitude is reached, *e. g.*, whether the height attained is rached by a slow and arduous climb, or whether the individual is transported thither passively either on horseback or on a train, or in a balloon or aeroplane flight.

Types of Mountain Sickness.—There are two types of mountain sickness, the acute and the chronic.

The *acute* type comes on when the transition from normal to low barometric pressure is abrupt, as when great heights are attained quickly either in a train or in a balloon or aeroplane flight. Generally speaking, the symptoms are characterized by rapid pulse, nausea, vomiting, dimness of vision, dulling of the hearing, buzzing in the ears, bodily weakness, which may reach such a degree as to render the subject incapable of movement, lividity of the skin, loss of consciousness, and death, if the barometric pressure falls too low or the exposure is too prolonged.

The more *chronic* or slow form of mountain sickness is the more usual type, and usually manifests itself when the altitude is reached by the usual process of mountain climbing, and does not greatly exceed the critical level above which symptoms are developed. On reaching such an altitude the individual complains of no symptoms at first, and on being questioned usually states that he feels well. He then occasionally experiences dizzy sensations, and spots seem to dance before his eyes, he has momentary dimness of vision, on straightening up quickly after stooping over. Although the subject still feels comparatively comfortable, inspection will usually show more blueness of the lips, gums, the ear-lobes and the finger-nails than is normal. Some hours later feelings of languor and depression begin to make their appearance, and the subject is disinclined to any exertion. The appetite is greatly diminished or is lost. Upon going to bed the subject feels weak and tired and usually has considerable difficulty in going to sleep. On waking up in the morning, after a bad night, there is usually a severe frontal headache which, in some instances, may have developed in the evening of the first day. The disinclination for food is increased to the extent of positive nausea or even vomiting, and on rising from the bed the subject feels distinctly giddy. The face has a dull and heavy expression, and is slightly cyanosed. The eyes are watery. The tongue is coated and the pulse is high, usually over 100. The temperature is normal, or there may be a tendency to a sub-normal temperature, which is manifested by chilly sensations. There are, perhaps, colicky pains in the abdomen; some diarrhea is present; and a tendency to periodic breathing has been noted. The mental efficiency is markedly reduced. The sufferer may show great unreasonableness of temper and may also experience great difficulty in performing mental processes such as multiplication or addition of numbers, which under ordinary circumstances are performed with ease. Barcroft recounts that at the altitude of 11,000 feet he heard two clever and distinguished physiologists pause to discuss whether or not 4 x 8 equaled 32.

According to the observations of Ravenhill * who was medical officer in the Andes in a mining district over 15,000 feet above sea level, mountain sickness of the normal type may be divided into two types: (1) those in which *cardiac* symptoms predominate; and (2) those in which *nervous* symptoms predominate.

---

* Ravenhill, T. H. "Some Experiences with Mountain Sickness in the Andes." *Jour. Trop. Med.*, London, 1913, xvi, pp. 313–320.

As an example of the first type he mentions the case of an Englishman who arrived in the district by train after a forty-two-hour journey from the sea level. This was not his first visit as he had lived there for three months and enjoyed good health all the time. He had also visited other mountains districts in Peru and had reached an altitude of 17,000 feet without inconvenience. Upon arrival he was apparently in good health and said that he felt quite well, although he remained quiet, did but little and went to bed early. He awoke the next morning with the usual symptoms of mountain sickness. As the day progressed, however, he became very ill; his pulse was very rapid, and respiration reached a rate of 144 and 40 respectively in the afternoon. Later on he was very cyanosed and suffered from acute air-hunger, all the extraordinary muscles of respiration being called into play. The heart sounds were very faint; the pulse was irregular and of small tension. He apparently presented a complete clinical picture of a failing heart. This condition persisted through the succeeding night, and was combined with difficulty in coughing up mucus. Inhalations of oxygen, strychnin and digitalis were administered. The patient was somewhat better towards morning and took advantage of an early morning train to return to a lower altitude. He was much better at 12,000 feet and at 7,000 feet was nearly well.

Ravenhill believes that had this patient persisted in remaining at the altitude of 15,000 or 16,000 feet he would have died. Ravenhill also cites the instance of another patient, a young Turk, aged twenty-three, who arrived in that district on July 14th and died on the 19th, after a similar history, the respirations being 60 and the pulse 144, the latter being hardly perceptible when examined by Ravenhill.

In the nervous type described by Ravenhill, the nervous symptoms are most prominent. The simplest form consists in the feeling of exaltation and buoyancy. It has been described as a sense of being lifted in the air as by a balloon. This sensation may precede an attack of mountain sickness of the ordinary type. There may be a tendency to the twitching of the lips and to the trembling of the limbs. While this form generally passes off, the nervous symptoms may be developed to an alarming extent.

Ravenhill reports one case of a young Chilean, aged 19, who three days subsequent to his arrival was found to be unable to speak, and to be seized with violent spasmodic movements of the extremities. He resisted examination and was unable to stand or walk. His face was blanched and his lips were almost white, the pupils of his eyes were slightly dilated. Temperature and respiration were normal; the pulse was 140. He had been in this condition practically ever since his arrival, being delirious and talking all kinds of nonsense. He was sent down to a lower altitude the same day and, by the time he had reached the coast, he had completely recovered. So far as the hemorrhages from mucous membranes were said to occur in cases of mountain sickness, Ravenhill states that epistaxis occurred in about 20 per cent. of the cases, but was hardly ever profuse. According to Ravenhill, while this is not very common in those arriving at such high altitudes, it seems to be a common symptom with all those living there when they become ill, especially with any febrile disturbance.

Before passing on to the discussion of the causes of mountain sickness, it is well to point out the dramatic suddenness with which symptoms may make their appearance where the transition to the altitude is continuous and rapid.

In the celebrated ascension on September 5, 1862, of Glaisher and Coxwell, the start took place at 1:03; at 1:39 the height of 6,437 meters (21,118.72 feet) was reached; at 1:51 the barometer marked 11.05 inches. Up to this time no difficulty had been experienced by Glaisher in making his observations of the instruments. Glancing at the barometer, he noted that it was but 10 inches, and was descending rapidly. On attempting to use his right arm, which up to that moment had had all its vigor, he perceived that it had lost all its power and on endeavoring to use his left arm, he found that it likewise was paralyzed. In endeavoring to move his body, he was able to succeed up to a certain point, but it seemed to him that he had no extremities. Trying once more to read the barometer, his head fell upon his left shoulder. Suddenly he felt unable to make any movements whatsoever. He was unable to speak to his companion, Coxwell. First he lost vision, then consciousness. Coxwell, unable to use his arms, pulled the valve cord of the balloon with his teeth and thus brought the aeronauts out of a situation which, if persisted in, would doubtless have been fatal to both.

Less fortunate were the results of the ascension of the "Zenith" which took place on April 15, 1875, in which three French aeronauts, Tissandier, Crocé-Spinelli and Sivel, endeavored to break the altitude record, with the result that of the three only Tissandier survived. The following translation from Tissandier's graphic account quoted in Paul Bert's book depicts this voyage in striking fashion and describes the insidious and abrupt onset of the effects of oxygen want at this high altitude.

"I arrive at the fatal hour when we were about to be seized by the terrible influence of low barometric pressure. At 7,000 meters (22,965 feet) we were all standing upright in the balloon basket; Sivel, torpid for a moment, had revived; Crocé-Spinelli is motionless facing me. 'See,' said the latter, 'how beautiful the cirrus clouds are * * * *.' The sky, far from being dark and black, was of a beautiful clear and limpid blue; an ardent sun burned our faces, nevertheless the cold commenced to make its influence felt and we had already before this placed our wraps on our shoulders. Torpidity had seized me, my hands were cold and icy. I wished to put on my fur gloves, but without being aware of it, the effort to take them from my pocket was one which I could not make.

"Nevertheless, at a height of 7,000 meters I write almost mechanically in my note book. I reproduce here the following lines which I wrote without having been actually conscious of writing them. They are written in almost illegible fashion by a hand which the cold must have caused singularly to tremble. 'My hands are frozen. I feel well. We all feel well. There is fog on the horizon with little rounded cirrus clouds. We ascend. Crocé pants. We breathe oxygen. Sivel closes his eyes. I empty the aspirator. The temperature —10°. 1 hr. 20 minutes. H = 320. Sivel is dozing. 1 hr. 25 minutes. Temperature —11°. H = 300. Sivel throws ballast Sivel throws ballast.'

"Sivel, indeed, who had remained some instants as though pensive and motionless, closing his eyes sometimes, without doubt having just recalled that he wished to transcend the limits where the 'Zenith' was floating, stood up. His energetic face lit up suddenly with an unaccustomed brightness, and he turned to me and said: 'What is the pressure?' '30 centimeters [7,450 meters (24,442 feet) of altitude].' 'We have much ballast; must we throw it out?' I answered him, 'Do what you wish.' He turns to Crocé with the same question. Crocé nods his head with an energetic sign of affirmation * * * * (Three sacks of ballast were then thrown out).

"But I had always kept my immobility without being aware that I had already lost the power of all movement. At 7,500 meters (24,606 feet) the state of torpidity in which one finds one's self is extraordinary. The body and mind become enfeebled, little by little, gradually, insensibly, without one's being aware of it. There is no suffering; on the contrary one feels an inward joy and, as it were, an effect of the radiation of light in which one is immersed. One becomes indifferent; one thinks no longer either of the perilous situation or of danger. One ascends and is happy in the ascension. The vertigo of the high regions is not an empty word but, in so far as I may judge by my present impressions, this vertigo appears as a last incident. It immediately precedes direct annihilation, sudden, unexpected, irresistible."

When Tissandier recovered consciousness, the balloon was descending with a frightful rapidity and his two companions were in the bottom of the balloon basket. Sivel's face was black, his eyes were glazed and his mouth open and full of blood; Crocé's eyes were half closed and his mouth bleeding. When the balloon finally reached the earth, his two companions were found to be dead.

The Cause of Mountain Sickness.—The cause of mountain sickness is oxygen want. That this condition was the cause of mountain sickness was first suggested by Jourdanet and subsequently demonstrated by Paul Bert.

Since the symptoms of mountain sickness are produced by oxygen want and by nothing else, some discussion is necessary of the mechanism of the physiological supply of oxygen to the tissues and of the relations of the partial pressure of oxygen in the atmosphere in effecting and maintaining the supply.

Mechanism of Oxygen Supply to the Tissues.—As is well known, the oxygen is carried to the body tissues by the hemoglobin in the red blood-cells. The venous blood as it circulates through the lungs is exposed to the air in the air-cells of the lungs, only a thin membrane intervening. The excess of carbon dioxid with which the venous blood is charged passes out into the alveolar atmosphere and oxygen unites itself to hemoglobin, thus converting the venous into artificial blood. Now the study of the ability of the hemoglobin to take up and to part with oxygen shows that it is one of the most remarkable substances in nature from a physical-chemical standpoint. While it is true that analogies have been attempted between the reactions of hemoglobin with oxygen and certain other chemical reactions, such as, for instance, the union of calcium oxid with carbon dioxid, nevertheless, such reactions are not analogous with the saturation or desaturation of hemoglobin with oxygen according to whether it becomes charged with oxygen in the lungs or gives up this charge to the tissues. Barcroft speculates that were it not for this remarkable quality of hemoglobin "man might never have attained any activity which the lobster does not possess, or, had he done so, it would have been with a body as minute as that of the fly." The properties of hemoglobin in its capacity to unite with oxygen are so remarkable that it is well worth our while to discuss them here briefly. It is well known that hemoglobin is a complex proteid iron-containing substance which has the property when shaken up with oxygen of uniting with a definite quantity of the gas, in the proportion of 32 grams (493.82 grains) of oxygen to each 56 grams (864.215 grains) of iron in the hemoglobin when fully saturated. When, however, we examine blood taken from the circulation, we always find it to be combined with a less quantity of oxygen than this.

This result, however, can be obtained only on condition that the hemoglobin with which we are experimenting is pure hemoglobin and nothing else, all salts of the plasma and all carbon dioxid being absent. An analysis of this curve shows that such a form of curve is unsuited to meet the requirement of the oxygen supply of the body, for while pure hemoglobin takes up oxygen very readily even at low pressures (*i. e.*, at 20 mm. pressure, the hemoglobin would still be approximately 70 per cent. saturated), it holds its oxygen too tenaciously to yield it readily to the tissues. We find, however, that in the case of the blood itself, the form of this curve which shows the percentage saturation of the pure hemoglobin with oxygen at various oxygen pressures is modified as follows: (*a*) by the presence of the salts in the blood; (*b*) by various pressures of carbon dioxid present; and (*c*) generally speaking, by the hydrogen-ion concentration of the blood. As a result of the numerous investigations which Bohr, Barcroft, Douglas, Haldane and others have carried on, the relation of the degree of saturation of hemoglobin with oxygen in the blood to the oxygen pressure, or, as it is termed, the "dissociation curve" of hemoglobin, is represented by the curve (Chart 4) from Barcroft which shows the limits within which the dissociation curves of normal persons fall.*

---

* Barcroft. Respiratory function of the blood. Page 226.

It will be seen that this curve is not a hyperbola but an S-shaped curve. It differs from the curve of saturation of pure hemoglobin with oxygen in two main respects: (1) that the percentage saturation is not so great with high oxygen pressures; and (2) oxygen is much more readily given up as the pressure falls. While, therefore, with a given oxygen pressure saturating the blood in the lungs, we do not get such a high percentage of oxygen taken up as in the previous case, on the other hand, the oxygen taken up is very much more readily given up to the tissues where the oxygen pressure is low and in this way the oxygen required for metabolism is more readily made available. It is to be observed that this curve which is a composite curve is rather broad and indicates considerable variation in the dissociation curves of normal individuals. The curves of particular individuals may move in either of two directions. Their blood at a given oxygen pressure may take up either more or less oxygen than the normal. Barcroft uses the following nomenclature to express these conditions; when the dissociation curve for a particular individual is above the normal situation, *i. e.*, when at a given oxygen pressure the blood takes up an abnormally great percentage of the total possible load of oxygen, the curve is called "pleonectic"; when it takes up less than the usual percentage of oxygen, it is "mionectic"; and when it becomes saturated to the normal extent, it is "mesectic." * The presence of both salts and acids has a similar effect on the oxygen dissociation curve of hemoglobin, but the

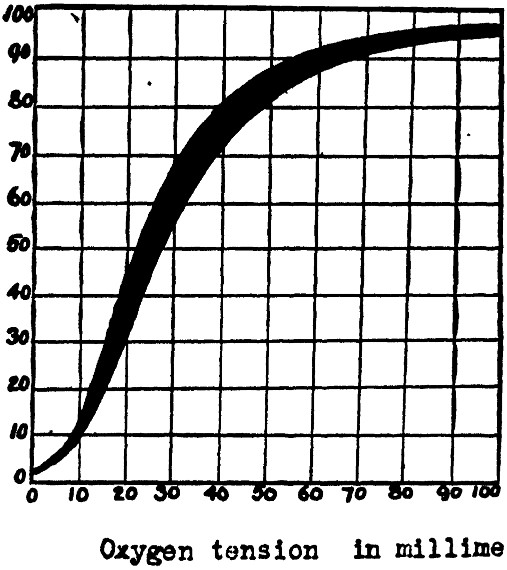


CHART 3.—NORMAL OXYGEN DISSOCIATION CURVE OF HEMOGLOBIN IN BLOOD. The thick line shows the extent of variation of normal curves in individuals. (After Barcroft.)

---

* Barcroft gives as a derivation of these adjectives the Greek word "Pleonektikos," disposed to take more than one's share, from "Pleonexia," a disposition to take more than one's share.

effect of acids is more marked than that of salts. Investigation has shown that this effect is due to the hydrogen ions present. The physiological importance of this modification is obvious. All cells produce carbon dioxid in activity, and as a result of muscular exertion lactic acid is formed. The presence of both of these facilitates the transfer of oxygen to active body cells.

Christianson, Douglas and Haldane have shown that reduced hemoglobin can take up one-tenth more carbon dioxid than hemoglobin fully saturated with oxygen. For this reason venous blood can take up more carbon dioxid at the same tension than can arterial blood. Since the affinity of hemoglobin for carbon dioxid diminishes as it absorbs oxygen, the carbon dioxid present in the venous blood is more readily given up in the lungs. Therefore, each gas assists in driving off the other. The form of this dissociation curve has been found to be related to the concentration of hydrogen ions in the blood, so that it may be used as an indicator for changes occurring in the hydrogen concentration in the blood, either as the result of exercise, of oxygen want, or of pathological states of so-called "acidosis."

The Lungs.—We have just seen how, through the unique property of hemoglobin, oxygen is conveyed to the tissues in far greater quantity than if it were merely dissolved in the blood-plasma, and how oxyhemoglobin parts with its oxygen at places in the body where the existing tension of oxygen gas is lower than at the point at which the hemoglobin took up its oxygen in the first place. In order to understand better the conditions of oxygen supply to the body which must be met under conditions of lowered atmospheric pressure, we must discuss the mechanism by which hemoglobin, after having given up the major part of its oxygen to the tissues, renews its supply from the external air, and at the same time gets rid of the carbon dioxid which has been given off to the hemoglobin by the cells. It is well known that carbon dioxid is transported from the tissues almost entirely by hemoglobin, the same substance which supplies the tissues with oxygen. Man, in common with other air-breathing animals, has an arrangement, the lungs, by which a large surface of blood is brought into contact with air, a thin membrane intervening between the blood and the air. This air is repeatedly changed by the process of breathing. The distance, therefore, through which the gases have to diffuse is extremely small. The air with which the blood is brought in contact is that contained in the sac-like terminations of the branching air tubes of the lungs, the pulmonary alveoli. Since it is mechanically impossible to empty all the air from the lungs, the air in these sacs is renewed by process of diffusion with the inspired air. Since oxygen is constantly being absorbed from it by the blood and carbon dioxid given out, this air contains oxygen at a lower pressure than the external air and carbon dioxid at a much higher tension than the external atmosphere. It is the alveolar air which actually takes part in the exchange of gases from the blood. Under ordinary conditions, at sea level, the composition of alveolar air is approximately from 13 to 14 per cent. of oxygen and from 5.5 to 6 per cent. of carbon dioxid. The approximate tension of the oxygen (allowing for the tension of water-vapor with which alveolar air is saturated) is 100 mm., while part of the carbon dioxid is 40 mm. This 100 mm. represents the pressure head under which oxygen enters the blood under ordinary conditions.

We may now discuss the physiological adaptations wrought in the body by exposure to diminished oxygen tension. These are:

(*a*) Changes in the respiration.
(*b*) Changes in the circulation.
(*c*) Changes in blood concentration.
(*d*) Possible changes in the oxygen tension of arterial blood.
(*e*) Changes in the acid-alkali balance of the blood.

CHANGES IN THE RESPIRATION BROUGHT ABOUT BY EXPOSURE TO DIMINISHED ATMOSPHERIC PRESSURE.—One of the most striking experiences of those obtaining high altitudes is the excessive panting which accompanies physical exertion. This panting is undoubtedly caused by a demand for oxygen in the body, and is a compensatory phenomenon. As is well known, under ordinary conditions the breathing is so regulated as to maintain the tension of the carbon dioxid in the alveolar air at a constant level (about 40 mm. for adults). Under ordinary conditions upon muscular exertion the amount of carbon dioxid carried to the lungs by the blood is very greatly increased, and therefore there is an increase both in the number and in the volume of respiration in order that the excess of carbon dioxid brought by the blood may be carried away.

We have seen that under ordinary conditions with a tension of about 40 mm. of carbon dioxid in the alveolar air, the corresponding oxygen tension of the air is about 100 mm. or approximately 13 per cent. of an atmosphere. While the changes in the hydrogen-ion concentration of the blood is the fundamental factor in exciting the respiratory center, under ordinary conditions respiration is regulated by the tension of carbon dioxid in the blood, changes of which produce variations in the hydrogen-ion concentration. There is such relation between the ventilation of the lungs, the excretion of carbon dioxid and the oxygen needs of the body as to maintain the tension of the carbon dioxid in the alveolar air at approximately the level noted above (40 mm.). When, however, there is increased demand for oxygen by increasing the ventilation of the lungs, we may not only wash out more rapidly the excess of carbon dioxid, as in the case of muscular exertion, but the increased ventilation will raise the tension of the oxygen in the alveolar air. Since the atmospheric air contains only 21 per cent. oxygen, it is impossible by any rate of pumonary ventilation to raise the percentage of oxygen in the alveolar air up to more than approximately 19 per cent. Since this is the case, it is evident that there is a limit to the extent to which increase in pulmonary ventilation may be counted on to raise the tension of the oxygen in the alveolar air of the lungs. Thus at an altitude of 14,000 feet (a barometric pressure of 460 mm.), the oxygen tension in the external air would be one-fifth of the barometric pressure, or 92 mm., and the utmost obtainable oxygen pressure in the lungs by the process of pulmonary ventilation could not exceed about 75 mm. (allowing for the pressure of water vapor in fully saturated air), and this pressure could be obtained only as a result of extraordinary panting which could not be maintained for any length of time. Observations show that at this elevation, the oxygen tension in the alveolar air is very far short of this level. Thus, Douglas, Haldane, Henderson and Schneider found that the tension of oxygen in the alveolar air at the summit of Pike's Peak averaged from about 53 to 56 mm. It is known that at sea level the percentage of carbon dioxid in the alveolar air remains approximately constant under all conditions. If, on increasing our altitude, the tension of carbon dioxid in the alveolar air were to remain constant at 40 mm., the percentage of carbon dioxid in the alveolar air would increase as the barometric pressure decreased. With increases in altitude this percentage of carbon dioxid would be so great as to lower the tension of oxygen to a point where the blood would be prevented from obtaining an adequate load of oxygen. We therefore find a fall in the tension of the carbon dioxid in the alveolar air as the altitude increases.

While undoubtedly the phenomenon of increased ventilation of the lungs as barometric pressure diminishes serves as a part of the compensatory mechanism to enable the body to obtain oxygen under conditions of increasing difficulty, simple increase in the rate of breathing is by no means sufficient to enable the fullest possible degrees of adaptation to be obtained. Mosso laid great stress upon the fall of the carbon dioxid pressure in the alveolar air because this would be an index of lowered carbon dioxid tension throughout the body generally. Since the reduction of carbon dioxid tension in the blood, all other things being equal, increases its affinity for oxygen, this by itself would be of material advantage in meeting conditions imposed by diminished barometric pressure. The diminution of the carbon dioxid tension would have the effect of increasing the alkalinity of the blood; this explains its greater affinity for oxygen. We are met here, however, with the difficulty that the greater oxygen affinity caused by the relative alkalinity would be more than offset by the reluctance with which hemoglobin parts with oxygen under conditions of diminished acidity. However, careful studies of the dissociation curve of the blood for oxygen by Barcroft and others show that this greater affinity of the blood for oxygen in the presence of lowered carbon dioxid tension incident to sojourn at high altitudes does not take place, and suggest that the missing carbon dioxid has been replaced by other substances, so that the acid-alkali balance of the blood is maintained at a constant level. Indeed, careful measurements have shown that under conditions of low barometric pressure, the increase in acid is slightly in excess of the loss of carbon dioxid. This increase in acid, while it would lower the affinity of the blood for oxygen, on the other hand would enable it to give up oxygen with greater readiness to the tissues, and this is, after all, the change which we desire to effect, as any slight loss in the affinity of the blood for oxygen can readily be compensated for by the great variations which can be had in the rate of circulation.

Periodic Breathing at High Altitudes.—Besides the increase in the rate of breathing in the lungs, there is one other tendency which we must mention and that is the tendency to periodic breathing at high altitudes. This type of breathing is frequently observed and is more marked in certain individuals than in others. In this type of breathing, the respirations occur in groups of three or four breaths, each succeeding breath being deeper than the preceding one, the interval between each group being marked by a pause. Again, the periodic breathing may occur in cycles of from six to ten breaths, each increasing in depth up to a certain point, after which the breathing again progressively diminishes, no pause, however, occurring. This type of breathing is especially marked on arriving at a high altitude, and tends to disappear as the process of acclimatization is effected. The respiration of oxygen will also abolish the periodic breathing. In those who have become more or less acclimated, this type of breathing disappears, but will often make its reappearance upon any exertion or upon holding the breath.

In this connection, it should be remarked that the ability to hold one's breath is markedly diminished at high altitudes, especially as the process of acclimatization becomes advanced. It has been suggested that the ability to hold the breath decreases as the acidity of the blood increases.

Changes in the Blood.—The blood reacts to diminished barometric pressure by an increase in the amount of hemoglobin present. It was first predicted and subsequently found by Paul Bert that one of the effects of continued exposure to diminished barometric pressure would be an increase in the hemoglobin of the blood. Subsequent observations have shown that this is true. More remarkable is the fact that these changes in the hemoglobin content of the blood are very rapidly produced.

Since these changes in the concentration of hemoglobin make their appearance very rapidly, one cannot suppose that they are produced by any immediate increase in the actual number of red blood-cells. The early evidence of hemoglobin percentage, therefore, can be produced only in two ways: (1) by an increase in the concentration of the blood, owing to a diminution of its volume; and (2) by the mobilization in the general circulation of red blood-cells which, under ordinary circumstances, are retained in the byways of the body. Thus, Schneider and Hagans state that abdominal massage and physical exertion often at low altitudes will cause an increase in the number of red cells in the hemoglobin in the peripheral capillaries, whereas in persons acclimatized to high altitudes abdominal massage produces no change (except a frequent lowering) in the contents of hemoglobin and red blood corpuscles; physical exertion fails to increase it. It would appear that the initial increase in hemoglobin observed at high altitudes at first is due in part to concentration of the blood, and in part to mobilization of dormant red blood-cells. The later changes are due to active formation of new blood elements. Thus Lequer found that dogs, bled to the extent of half their hemoglobin, regenerated fully in about 16 days on Monte Rosa, whereas at a lower altitude about 27 days were required before restoration after a similar hemorrhage.

The natural effect of this increase in hemoglobin is to increase considerably the oxygen capacity of the blood, thus we note that in the Pike's Peak experiments the increase in the total oxygen capacity of the blood in the case of Haldane was 21 per cent.; in the case of Henderson from 35 to 40 per cent.; and in the case of Schneider about 27 per cent. It can readily be seen that these changes in the hemoglobin of the blood must be an important factor in the process of adaptation to life at low barometric pressures.

Changes in the Circulation.—As is well known, the rate of circulation in the human body may be subjected to great changes. Thus while a round of circulation takes place in about one minute in the resting individual, under severe muscular exertion the time of a round may be reduced to ten seconds. Moreover, the dilatation of the blood-vessels and capillaries may enormously increase the amount of blood-flow through a part. The circulatory mechanism of the body is very sensitive to oxygen demand, the call for oxygen by the various cells of the body being responded to rapidly, and the flow through the tissues requiring an increased supply is itself greatly increased. We thus find the circulation playing a very important part in meeting the difficulties of supplying oxygen in the face of diminishing barometric pressure. The strain thrown upon the circulation in meeting these demands when they are severe also points to the explanation why it is that persons with cardiac defects are unable to adapt themselves satisfactorily to the conditions of life at diminished barometric pressure.

The changes in the circulation due to diminished barometric pressure are reflected in the pulse-rate, the arterial pressures, the capillary pressure, and the venous blood-pressure. Some work has also been done in the way of determining, indirectly, the output of the heart for each beat, and the rate of blood-flow through the lungs and other tissues.

The Pulse-rate.—The acceleration of the pulse due to exposure to low barometric pressures is one of the most conspicuous of the responses to diminished barometric pressure. In the studies made by the Medical Service of the Division of Aeronautics, U. S. Army, during the war, it was found that a study of the pulse-rate during exposure to low oxygen pressures gave a definite indication of the sensitiveness of the organism to low oxygen tension, provided care was taken at the beginning of the experiment to have the subject quiet and calm. The response of the circulation to diminishing barometric pressure is especially important in the case of aviators, as in flying they are transported rapidly to high elevations and the adaptation made to the existing low barometric pressure must therefore be brought about by the emergency adaptive mechanism of the body without a process of acclimatization being called into play. As a result of a careful study by the Service of the reaction of the pulse to barometric pressure, it was found that in a very few individuals the rate of heart beat began to accelerate when the oxygen was reduced only to 17.5 per cent. (5,000 feet altitude).

In a group of 70 individuals the following reactions were abserved:

1 per cent. began to react between 7,000 and 8,000 feet (15½ per cent. oxygen).
12 per cent. began to react between 8,000 and 9,000 feet (from 15.5 to 14.9 per cent. oxygen).
20 per cent. began to react between 9,000 and 10,000 feet (from 14.9 to 14.2 per cent. oxygen).
14 per cent. began to react between 10,000 and 11,000 feet (from 14 to 13.7 per cent. oxygen).
23 per cent. began to react between 11,000 and 12,000 feet (from 13.7 to 13.2 per cent. oxygen).
20 per cent. began to react between 12,000 and 13,000 feet (from 13.2 to 12.7 per cent. oxygen).
6 per cent. began to react between 13,000 and 14,000 feet (from 12.7 to 12.2 per cent. oxygen).

The increase noted in the heart beat is at first only from one to three beats per minute, but as the oxygen tension progressively decreases, a greater increase in the rate is likely to occur for each successive diminution in the oxygen. A very marked increase in the acceleration in the pulse takes place as the oxygen tension falls from 13 to 9 per cent. of an atmosphere. In certain individuals, after the more rapid acceleration of the pulse sets in, a satisfactory increase in the rate takes place down even to 6½ or 6 per cent. of oxygen, while in others, after a period of rapid acceleration, the rate of the acceleration becomes less for each decrement of oxygen. This decrease in the rate of acceleration suggests that for such individuals the maximum of adaptation has been reached. Some individuals after reacting with good acceleration soon reach a rate beyond which decrease in the oxygen tension will produce no further acceleration. In such cases the heart, after beating at a fixed rate, begins to slow, a sure indication that the limit of adaptation has been reached.

In these experiments it was found that a total increase of from fifteen to forty beats in the heart rate during a test in which the oxygen was lowered to between 7½ and 6½ per cent. of an atmosphere constituted a good reaction to oxygen want. A failure to react in the pulse-beat may mean either inability to compensate for low oxygen pressure, or it may indicate that the situation has been met in other ways, either through increased ventilation or concentration of the blood. The general experience was, however, that the failure of the pulse-rate to react was an indication of poor toleration of low oxygen tension. An acceleration of more than forty beats in the heart rate was indicative of too great a strain on the circulation and was met with only in men who did not tolerate well low percentages of oxygen.

Blood-pressure.—The changes produced in the blood-pressure by exposure to diminished barometric pressure are by no means striking. A little reflection shows clearly why this is so.

We have seen that the pulse-rate is a rather sensitive indicator of the response of the body to oxygen want. We must consider the fact, too, that when there is a call for oxygen in the tissues there is a dilatation of the arterioles and thus an increase in the amount of blood brought to the tissues. We would expect that the blood-pressure at the level characteristic of the individual would be maintained at more or less its normal level so long as the circulatory system was adequately meeting the demands upon it in maintaining circulation. So long as good compensation is maintained, there should be no striking changes in either the systolic or the diastolic blood-pressures. The Army studies previously referred to showed certain definite trends of the effect of low oxygen tensions on the circulation with regard to the systolic or diastolic blood-pressures. The systolic pressure maintained its normal level in the majority of cases; in 25 per cent. of the cases a rise occurred during the first part of the experiment, and a gradual fall was noted as the experiment proceeded. In others a gradual fall began soon after the desired altitude was attained. So far as the diastolic pressure is concerned, this usually fell gradually from 4 to 28 mm. while the subject was being held at a given low oxygen tension. In many experiments, as time went by, the diastolic pressure tended to return to the normal. In other cases the diastolic pressure continued to fall gradually throughout the entire experiment. In a few men the pressure was unaltered by the low oxygen tension. It follows that the pulse pressure usually increased during the time of holding at low oxygen tension as the changes in the pulse pressure are inverse to the diastolic pressure. In subjects who reacted poorly, both the systolic and the diastolic pressures fell, the diastolic pressure falling greatly immediately before the subject became entirely inefficient. Since on the one hand, therefore, we have (1) rather satisfactory maintenance of the systolic and diastolic blood-pressures, (2) a very definite acceleration of the pulse-rate, (3) a very pronounced diminution of peripheral resistance because of dilatation of the arterioles and capillaries in order to supply the tissues with more oxygen through an increased blood supply, it is justifiable to assume that the output of the heart per minute is very definitely increased during exposure to diminished barometric pressure. Confirmatory evidence of this is shown by the observations of Schneider and Cisco on Pike's Peak where by the use of Stuart's hand colorimeter they determined that the circulation in the hands of subjects which they observed was increased from 50 to 70 per cent.

CORRELATION OF THE COMPENSATORY FACTORS.—We have seen from the foregoing that three of the main responses to diminished barometric pressure are:

(1) Increase in the ventilation of the lungs.

(2) Increase in the pulse-rate.

(3) Increase in the hemoglobin content of the blood: through (*a*) concentration at first, and (*b*) through formation of new blood elements.

Studies made by Gregg, Lutz and Schneider at the Medical Research Laboratory of the Army Air Service at Mineola, New York, show that the variations that are produced in the reactions to low barometic pressure in different individuals are related to the relative prominence of each of these responses. Thus, with rapid concentration of the blood and the rise in its hemoglobin content, we may get a less decided response to diminished oxygen tension in the way of increased pulse-rate and increased ventilation of the lungs. Again, in cases where the response was characterized by an abnormal increase in the pulse-rate, the evidence of concentration of the hemoglobin did not take place. Other subjects produced an unusual amount of compensation by raising the tension of the oxygen in the alveoli of the lungs by excessive pulmonary ventilation, nor was the response constant on all occasions for the same individuals, as the records of the experiment show that one individual at least reacted in a different way on each of four separate occasions.

Gregg, Lutz and Schneider classify the compensation during exposure to low oxygen tension as follows: (*a*) Those in which the pulse, after maintaining a high rate for a while, retards slowly and the percentage of hemoglobin increases; (*b*) those in which the pulse, after a preliminary rise, maintained a constant rate while the hemoglobin increased; (*c*) those in which the pulse-rate, after the preliminary rise, remained constant and in which the hemoglobin did not increase; (*d*) those in which the pulse-rate, after a preliminary rise, retarded and the hemoglobin did not increase. They give the following percentage of these various classes of reactors: (*a*) 55 per cent.; (*b*) 19 per cent.; (*c*) 17 per cent.; and (*d*) 9 per cent. They point out that the interdependence of the three compensatory reactions was shown also in a few cases in which the increase in the pulmonary ventilation, following a period of equilibrium in circulation and respiration, resulted in a retardation in pulse-rate and blood-flow.

THE ARTERIAL OXYGEN TENSION IN EXPOSURE TO THE DIMINISHED BAROMETRIC PRESSURE.—Up to the present time we have considered the respiratory and circulatory response to diminution in the barometric pressure and have considered that whatever the call for oxygen by the body cells, the blood took up in the lungs all the oxygen it could obtain by a process of simple diffusion through the epithelium lining the alveoli of the lungs, increased pulmonary ventilation bringing about a reduction in the tension of the carbon dioxid present in the alveolar air and making available for the process of diffusion a larger proportion of existing oxygen tension.

When the tension of the blood gases was investigated by aërotonometric methods by the physiologists of the Bonn School, no other view was held than that the blood obtained its load of oxygen by a process of simple diffusion through the pulmonary epithelium. Bohr, as the result of some experiments in which he apparently found that there was a greater pressure of oxygen in the arterial blood than in the alveolar air and conversely a greater pressure of carbonic acid in the alveolar air than in the arterial blood, put forth the theory that instead of a simple process of diffusion being called into play, the pulmonary epithelium had the ability to actively secrete oxygen inwards into the blood, and to excrete carbon dioxid into the alveolar air of the lungs. Further, by a mathematical analysis of the process of diffusion through a moist membrane, Bohr arrived at the conclusion that with diffusion alone a difference of pressure of at least 25 mm. on opposite sides of the membrane would be required. Under these circumstances, the diffusion theory would be inadequate to account for the oxygen consumption of the body under all conditions. Now there is nothing inherently improbable in this theory of Bohr's as physiologists are well acquainted with other analogous processes, as for instance the secretion of oxygen by the epithelium of the swim bladder of fishes, *e. g.*, the swim bladder of the cod fish, if emptied, gradually refills and the gas on analysis contains some 80 per cent. of oxygen. If, as Barcroft remarks, the swim bladder of the cod fish has this power, if the cells of the stomach can secrete hydrochloric acid, there is no reason why the epithelium of the lungs should not secrete oxygen. Of course, those who are in favor of the diffusion theory proclaim that simple diffusion is inherently the more probable because to their minds it is the simpler process, yet to the biologist it would seem just as probable that certain cells of the body should take on specialized functions as that they should act as pieces of inert animal membrane. The oxygen secretion theory has received further impetus by the work of Haldane and Lorraine Smith, and subsequently by Haldane and Douglas This work has had great influence on physiological thought in the past decade. In their method of investigating the oxygen arterial tension, Haldane and Lorraine Smith made use of the following facts. If hemoglobin is exposed to a mixture of carbon monoxid and oxygen, oxy- and carbo-oxyhemoglobin will be formed in proportion to the relative tensions of oxygen and carbon monoxid. In other words, there is a balanced reaction, thus:

$$CO + O_2Hb \rightleftarrows COHb + O_2$$

If any three of these quantities can be determined, the fourth can be calculated. In the method developed by Haldane and Douglas a known amount of carbon monoxid is administered by a special apparatus, enough to saturate the blood of the subject to approximately 20 or 21 per cent. The subject then breathes into a closed space, arranged on the Regnault-Reiset principle, by which the carbon dioxid is absorbed as it is exhaled, and oxygen is automatically added to make up for that used by the subject. As carbon monoxid, except for its affinity for hemoglobin, is physiologically inert, and therefore diffuses indifferently backwards and forwards through the pulmonary epithelium, in a short while the tension of the carbon monoxid in the blood and that in the air in the closed space which is being breathed into by the subject will come to an equilibrium. A sample of blood is then taken from the subject, defibrinated, and a small portion of it exposed to the air of a saturating chamber which is filled with the air that the subject has been breathing plus an amount of carbon dioxid to make the tension of carbon dioxid in the air of the saturating chamber equal to that in the subject's alveolar air, as determined by examining a sample of the alveolar air. Since the percentage of carboxyhemoglobin present in the blood at a given tension of that gas is dependent upon the tension of oxygen in the blood, a little reflection will show us that if the blood exposed in the saturator takes up a greater percentage of carbon monoxid than is present in the blood examined immediately upon withdrawal from the individual, then the oxygen tension of the arterial blood must be higher than that in the alveolar air, and conversely if the percentage of carboxyhemoglobin is greater in the sample from a subject than in the blood exposed in the saturator, then the oxygen tension of the arterial blood is lower than that of the inspired air. Using this method, Haldane and Douglas obtained evidence that under conditions of oxygen demand such as those produced by prolonged muscular work, inhalation of carbon monoxid or exposure to low oxygen pressure, secretory action of the pulmonary epithelium took place.

In the meantime, Krogh, by his beautifully devised micro-aërotonometric methods, had shown that Bohr had been in error in his analysis of the physical laws governing diffusion through the pulmonary epithelium and instead of 25 mm. of available oxygen tension being absorbed in the process of diffusion, that this number was relatively small, somewhere in the neighborhood of 2 or 3 mm. In the meantime, Haldane and his co-workers had revised their view to the extent that they did not believe any active secretion of oxygen by the pulmonary epithelium took place under ordinary circumstances, but that this secretory activity was called into play (*a*) either when unusual demands were made for oxygen by the body, or (*b*) when difficulties existed in furnishing an adequate supply. Thus by the carbon monoxid method they obtained no evidence of oxygen secretion by the pulmonary epithelium when the body was at rest or when the air breathed contained a high percentage of oxygen. On the other hand oxygen secretion is evidenced by increase in tension of the oxygen in the arterial blood either when low percentages of oxygen were breathed or when severe muscular work was being performed. Further evidence of oxygen secretion under conditions of oxygen want was obtained by the result of Douglas, Haldane, Henderson and Schneider on Pike's Peak where, using this method, they found consistent evidence of oxygen secretion.

On the other hand, recent evidence would tend to show that the question of active oxygen secretion by the pulmonary epithelium must still be regarded as *sub judice*.

CHANGES IN THE ACID-ALKALI BALANCE OF THE BLOOD.—Finally, there remains for discussion the effects of exposure to diminished barometric pressure upon the acid-alkali balance of the body and the manner in which changes in this balance are reflected by the dissociation curve of hemoglobin for oxygen. Since the regular effect of ascending to a high altitude is to diminish the tension of the carbon dioxid present in the alveolar air, and consequently in the blood, in the absence of any other compensatory change, the deficit in carbon dioxid would lower the hydrogen-ion concentration of the blood and hence render it more alkaline. This would increase the affinity of hemoglobin for oxygen and we would expect that the dissociation curve of the individual's blood would be found displaced to the left upon ascending to a high altitude. Yet much modification of the affinity of the blood for oxygen brought about by lowered hydrogen-ion concentration would by no means be advantageous, for though the affinity for oxygen is increased, the hemoglobin parts with oxygen to the tissues much less readily. Moreover, since the respiratory center is stimulated by increases in the hydrogen-ion concentration, the diminished acidity of the blood would fail to stimulate the respiratory center to a degree of activity commensurate with the oxygen demands. Indeed, it is well known that by forced breathing the carbon dioxid may be washed out of the blood and its hydrogen-ion concentration lowered thereby to such an extent that apnea results and dangerous symptoms of oxygen want may supervene without any respiratory efforts being made by the subject of the experiment. The observations of Barcroft and others have shown us that change in the dissociation curve due to the carbon dioxid deficit does not take place on ascending to a high altitude. Consequently, the loss in acid caused by diminished tension of carbon dioxid has been replaced by other acid substances.

It has been shown by Barcroft that on the performance of muscular work the dissociation curve is affected by the lactic acid present in the blood so that it becomes displaced to the right, in other words the individual changes from the mesectic type to the mionectic type. This change is in the interest of the easy supply of oxygen to the tissues, for while it is true that blood does not become saturated with oxygen in the lungs to the former extent, on the other hand it parts with its oxygen to the tissues with much greater facility and the slight loss in degree of saturation from the lungs is more than made up for by the increased rapidity in the circulation. In muscular work at high altitudes the same effect is evident. Barcroft contrasts his generally depressed and let-down condition during the experiment at Teneriffe with his much greater feeling of comfort on Col d'Olen, and attributes the differences observed at similar altitudes to the fact that he reached his destination at Teneriffe on mule back, while on Col d'Olen the station was reached on foot. The result of the muscular exercise was to increase the hydrogen-ion concentration of his blood through the lactic acid produced, and hence render his blood dissociation curve mionectic. While the performance of muscular work, as in climbing a mountain, may diminish the effects of mountain sickness by the lactic acid produced, it must not be supposed, however, that the increase in hydrogen-ion concentration of the blood which is an effect of acclimatization to high altitudes is produced by lactic acid. The determination of lactic acid in the blood by Ryfel's delicate method has shown no increase in the lactic acid present in the blood in the resting individual at high altitude, although there must have been a definite increase in other acid substances in order to make up for the deficit in carbon dioxid, since the dissociation curve remained unchanged. Moreover, the mionectic condition produced by lactic acid consequent on exercise is but a temporary condition and passes off after a few hours' rest, for lactic acid is readily excreted by the kidneys. On the other hand, the increase in hydrogen-ion concentration of the blood, caused by sojourn in high altitudes, is a much more persistent condition, and will remain for some time after the individual has gone down again to a lower level.

To quote Barcroft the physiological significance of the mionexy and of the acidosis is as follows:

> "The essence of any mechanism of adaptation to high altitudes must be a 'speeding-up' of the whole process of respiration, physical and chemical. The blood in the lung is exposed to a lower oxygen pressure than usual; it is saturated to a less extent with oxygen than formerly. The tissues begin to suffer from oxygen want: a very trifling change in the blood is enough to produce a great change in the circulatory conditions; the pulse quickens, respiration becomes deeper and more rapid, the amount of blood which leaves the lung increases perhaps twofold. Let the reader picture to himself each corpuscle as a ship with its little cargo of oxygen and twice as many of these are leaving the lung as before; they go to the tissue and go through the capillary at perhaps twice their former velocity: but stay—how are they to unload their cargo in the reduced time at their disposal? How futile would be the whole scheme if the corpuscle bolted through the capillary carrying its oxygen into the vein with it. Here is the advantage of mionexy. The mionectic blood parts with its oxygen with much greater rapidity than does the normal blood under given circumstances. Therefore when the corpuscle gets to the capillary it can discharge its cargo with unusual facility."

Barcroft points out that while climbing to reach an altitude, the degree of acidosis actually present is greater than that shown by the dissociation curve, for the hydrogen-ion concentration of the blood is being increased in a twofold manner; first, by the acid substances produced to make up for the deficit in carbon dioxid lost through the diminished tension of carbon dioxid in the blood, and second, through the lactic acid produced by exercise. The natural effect of these conditions is to cause the blood to be slightly more acid than formerly, for while it is much poorer in carbon dioxid, it is much richer in other acids than before. This diminished amount of carbon dioxid in the blood reduces the percentage of carbon dioxid in the alveolar air and therefore raises the oxygen pressure in the alveolar air higher than otherwise would be the case. This increase in the oxygen tension of the alveolar air raises the rate at which blood can acquire oxygen and at the same time increases the degree of saturation, so that the lessened combining power of the blood with oxygen caused by the mionexy is more than offset by the increased tension of oxygen in the alveolar air, while very great advantage from this condition is gained by the increased facility with which the blood gives up its oxygen to the tissues.

Prevention of Mountain Sickness.—We have seen that there are wide limits in the tolerance of different individuals for diminished barometric pressure. Physical fitness, rich blood, a good cardiovascular system, nerve-centers which are sensitive to oxygen want, and ability of the blood to change its hydrogen-ion concentration to suit the conditions, seem to constitute the factors which enable one most readily to adapt himself to diminished barometric pressure. It is perhaps for this reason that we hear so little of the effects of mountain sickness from people who are fond of mountain climbing, for by the constant physical exercise involved the organism has been placed in the best condition to adapt itself to the fullest possible extent to changes in barometric pressure. It is for these reasons too that we divine how it is that persons out of condition, or suffering from cardiac defects or from anemia find great difficulty in adjusting themselves to diminished barometric pressure and are often unable to live even at moderate elevations. One must consider that even in the resting condition at a high altitude one is already partly out of breath, so that the oxygen required by any added muscular exercise must be provided by a body already working on a high plane of effort. Where great heights are attained in a passive way, as undoubtedly will be more frequently the case as the commercial use of the aeroplane develops, there can be no question of any process of acclimatization, as the exposures to diminished barometric pressure are not sufficiently long for any genuine acclimatization to become possible. Whatever adaptation is made must be accomplished by the emergency adaptive mechanism of the body. Observations made on aviators during the war showed no evidence of any real acclimatization even in aviators who frequently patrolled at great heights. On the contrary, they showed that accidents, mistakes in judgment, inefficiency, loss of memory of facts observed during patrols, sleeplessness and general decline in physical fitness made their appearance in aviators as a result of frequent flights at high altitudes which at first were borne without particular disturbance by the individual. Yet the conditions of aviation are such as to make it imperative for all engaged therein to maintain the fullest possible measure of physical and mental efficiency at all times. Fortunately the symptoms due to diminished barometric pressure may be abolished at any time by inhalations of oxygen gas. Such inhalations should be administered by properly devised apparatus through a properly fitting mask, and to be effective should be commenced before actual symptoms have made their appearance. The apparatus devised by Dreyer seems to be effective in this connection. It is designed to be continuously worn and the oxygen supply is regulated by aneroid adjustment so that the amount of oxygen supplied is increased as the barometric pressure diminishes. The importance of some such apparatus as this for the administration of oxygen when flying at high altitudes is all the greater because the aviator himself is rarely conscious of the extent to which his faculties have been benumbed by oxygen want. It is only upon inhalation of oxygen that he becomes conscious of the degree to which his faculties have been impaired. Thus the roar of the motor which, through dulling of the hearing, had been reduced to a faint hum, is perceived to its full extent. Sky which has appeared black again becomes a brilliant blue. All the faculties are revived to their normal vigor. The body once more recovers its former poise and certainty of action; muscular movements, which formerly appeared to require a gigantic effort, become ridiculously easy in contrast. Besides this, the headache, the extreme fatigue, the benumbed and dazed mental condition frequently observed on landing after flights at great altitudes, as well as the poor appetite fail to make their appearance, when oxygen inhalations are practised. For those who desire to indulge in mountain climbing or to live at high altitudes, attention to the laws of hygiene in placing the body in the best physical condition by means of suitable diet and exercise forms the best preliminary training. Where the contemplated sojourn is long and the altitude is high, the process of acclimatization will be furthered by a gradual ascent to the proposed level, sojourns of several days each at lower levels being undertaken.

BIBLIOGRAPHY

Conditions Due to Compressed Air

BABINGTON and CUTHBERT. Paralysis caused by working under compressed air in sinking the foundations of Londonderry New Bridge. Dublin Quart. Jour. Med. Sci., 1863, xxxvi, 312–318.

Bassoe, P. The late manifestations of compressed air disease. Am. Jour. Med. Sci., Phila. and New York, 1913, clxv, 526–542.

——— Tr. XV Inter. Cong. Hyg. and Demogr., Wash. (1912), 1913, iii, 626–638.

Bert, P. La préssion barométrique, recherches de physiologie experimentale. Paris, 1878, G. Massön.

Blanchard et Regnard. Sur les accidents de la décompression chez les animaux Soc. biol.; Gaz. med. de Paris, 1881, No. 21.

Boot, G. W. Caisson workers' deafness. Ann. Otol., Rhinol. and Laryngol., St. Louis, 1913, xxii, 1121–1132.

Bornstein, A. Ueber den Einfluss der comprimierten Luft auf die Blutbildung. Arch. f. d. ges. Physiol., Bonn, 1911, cxxxviii, 609–616.

——— Versuche über die Prophylaxe der Pressluftkrankheit. Berl. klin. Wchnschr., 1910, xlvii, 1272–75.

——— Physiologie und Pathologie des Lebens in verdichteter Luft. Berl. klin. Wchnschr., 1914, li, 923–928.

——— Erfahrungen über Pressluftkrankheit. Vierteljahrschr. f. gerichtl. Med., Berlin, 1912, n. F. xliv, 357–375.

Bornstein und Plate. Ueber chronische Gelenkveränderungen entstanden durch Presslufterkrankung. Fortschr. a. d. Geb. d. Rontgenstrahlen, Hamburg, 1911–1912, xviii, 197–206.

Boycott, A. E. Caisson disease. Quart. Jour. Med., Oxford, 1907–8, i, 348–375.

Boycott and Damant, G. C. C. On the blood volume of goats and its relation to their varying susceptibility to symptoms of caisson disease. Proc. Physiol. Soc. Lond., 1907, xiv.

——— Some lesions of the spinal cord produced by experimental caisson disease. Jour. Path. and Bact., Cambridge, 1907–8, xii, 507–515, 2 pl.

——— Experiments on the influence of fatness on susceptibility to caisson disease. Jour. Hyg., Cambridge, 1908, viii, 445–456.

Boycott, A. E., Damant, G. C. C., and Haldane, J. S. The prevention of compressed air illness. Jour. Hyg., Cambridge, 1908, viii, 324, 443, 3 pl.

Brand, J. D. Over ongevallen bij pneumatische fundeeringen. Nederl. Tijdschr. v. Geneesk., Amsterdam, 1905, ii, xli, No. 2, Part 2, 34–40.

Brize-Fradin. La chimie pneumatique appliquée aux travaux sous l'eau. Paris, 1808.

Brooks, H. An experimental study of caisson disease. Proc. New York Path. Soc., 1907–8, vii, 58–87.

Bucquoy. Actions de l'air comprimé sur l'économie humaine. Strasbourg, 1861.

Cassaet. Des accidents de l'entrée de l'air dans les veines comparés a ceux des ouvriers tubistes. Bordeaux, 1889.

——— De la pathogénie des accidents de l'air comprimé. Thèse de Bordeaux, 1886.

Catsaras. Recherches cliniques et expérimentales sur les accidents survenant par l'emploi des scaphandres. Arch. de Neurol., Paris, 1890, xix, 48–77; Paris, 1890, 328 p., 5 tab. 8°.

Citroen, S. Over het ontstaan van caisson ziekte. Nederl. Tijdschr. v. Geneesk., Amsterdam, 1908, i, 1916–1924.

Clark, E. A. Effects of increased atmospheric pressure upon the human body; with a report of thirty-five cases brought to the City Hospital from the caisson of the St. Louis and Illinois Bridge. Med. Arch., St. Louis, 1870–1871, v, 1. (*Also* reprint of paper.)

——— Diving manual, by authority of the Lords Commissioners of the Admiralty. London, 1907, li, 111. V. Schr.

Erdman, S. The acute effects of caisson disease or aeropathy. Am. Jour. Med. Sci., New York and Phila., 1913, clxv, 520–26; *Ibid.*, Tr. XV Internat. Cong. Hyg. and Demogr., Wash. (1912), 1913, iii, 619–25.

Ferrannini, L. Le alterazioni del sangue per affecto delle variazioni della pressione atmosferica. Riforma med., Napoli, 1914, xxx, 182–186.

Foley, A. E. Du travail dans l'air comprimé; étude médicale, hygienique et biologique faite au Pont d'Argenteuil. Paris, 1863.

French, G. R. W. Observations on deep sea diving. U. S. Nav. Med. Bull., Wash., 1915, ix, 227–253.

Greenwood, M. The effects of rapid decompression on larvæ. Jour. Physiol., Cambridge, 1906, xxxv.

——— The influence of increased barometric pressure upon man; saturation of the tissue fluids with nitrogen. Brit. Med. Jour., Lond., 1907, i, 373.

Greenwood, M., Jr. Arris and Gale lectures on the physiological and pathological effects which follow exposure to compressed air. Brit. Med. Jour., Lond., 1908, i, 914; 983.

Guerard. Note sur les effets physiologiques et pathologiques de l'air comprimé. Ann. d'hyg. pub. et de med. leg., Paris, 1884, 2 serie, Tome i, pp. 279–304.

Haldane, J. S. Work under pressure and in great heat. Science Progr. 20th Cent., Lond., 1907–8, ii, 378–398.

——— Some recent investigations in the hygiene of subterranean and subaqueous work. Trans. XIV Internat. Cong. Hyg. and Demogr., Berlin, 1907.

Halley, E. The art of living under water. Transactiones angl. (Cloche de Halley), Philosophical transactions, 1716, xxix and xxxi.

Ham, C., and Hill, L. E. Effect of increased carbon dioxid tension, together with increased atmospheric pressure. Proc. Physiol. Soc. Lond., 1905, p. 7.

——— Estimation of the gas set free in the body after rapid decompression from high atmospheric pressure. Proc. Physiol. Soc. Lond., 1905, p. 5; *Ibid.*, 1905, July 1, p. 6.

——— Oxygen inhalation as a means to prevent caisson and diver's sickness. Proc. Physiol. Soc. Lond., 1905, p. 6.

Heller, R. Die Caissonkrankheit; eine Monographie. Zurich, 1912, Leemann & Co.

Heller, R., Mager, W., and Schroetter, H. V. Luftdruckerkrankungen. Wien, 1900.

Hersent, H. .Travaux publiques. Paris, 1889, Imprim. Chaix.

——— Note sur l'emploie de l'air comprimé pour l'exécution des ouvrages hydrauliques et spécialement des fondations. Expériences faites à Bordeaux. Paris, 1895, Chaix.

Hill, L. E. Caisson sickness. Edward Arnold, London, 1912.

——— The physiology of submarine work. Rep. Brit. Assn. Adv. Sc., 1911, London, 1912, 634–647.

Hill, L. E., and MacLeod, J. J. R. Caisson illness and diver's palsy. An experimental study. Jour. Hyg., Cambridge, 1903, iii, 401–445.

——— The influence of compressed air on the respiratory exchange. *Ibid.*, 493.

——— The influence of compressed air and oxygen upon the gases of the blood. Jour. Physiol., 1903, xxix, 382.

Hill, L., and Greenwood, M., Jr. The influence of increased barometric pressure on man. Proc. Roy. Soc. Lond., 1907, Series B, lxxix, 21–27.

——— The influence of increased barometric pressure on man. No. III. The possibility of oxygen bubbles being set free in the body. Proc. Roy. Soc. Lond., 1907, Series B, lxxix, 284–287.

——— The influence of increased barometric pressure on man. No. IV. The relation of age and body weight to decompression effects. Proc. Roy. Soc. Lond., 1908, Series B, lxxx, 12–24.

——— The influence of increased barometric pressure upon man. Proc. Roy. Soc. Lond., 1905–6, Series B, lxxvii, 442–453.

——— On the formation of bubbles in the vessels of animals submitted to a partial vacuum. Jour. Physiol., Lond., 1910, xxxix, 23.

Hoppe, F. Ueber den Einfluss, welchen der Wechsel des Luftdruckes auf das Blut ausübt. Arch. f. Anat., Physiol. u. wissersch. Med., Leipzig, 1857, xxiv, 63–73.

Jaminet, A. Physical effects of compressed air, and of the causes of pathological symptoms produced on man, by increased atmospheric pressure employed for the sinking of piers, in the construction of the Illinois and St. Louis Bridge over the Mississippi River at St. Louis, Missouri. St. Louis, Mo., 1871.

Japp, H. Caisson disease and its prevention. Trans. XV Inter. Cong. Hyg. and Demogr., Wash. (1912), 1913, iii, 639–654.

Jourdanet, D. Influence de la préssion de l'air sur la vie de l'homme. Paris, 1876.

Keays, F. L. Compressed air illness. New York, 1909.

Lepine, J. Sur les lésions médullaires de la décompression brusque. Bull. Soc. de biol., Paris, Oct. 27, 1900.

LeRoy de Méricourt. Consideration sur l'hygiène des pêcheurs d'éponges. Ann. d'Hyg. pub. et de med. leg., Seconde Série, 1869, xxxi, 274–286.

McWhorter, J. E. The etiological factors of compressed air illness; the gaseous contents of subaqueous tunnels; the occurrence of the disease in workers. Am. Jour. Med. Sci., Phila. and New York, 1910, cxxxix, 373–383.

MacNaughton, G. W. F. Frictional electricity, a factor in caisson disease. Lancet, London, 1906, ii, 435.

Musenga, G. Un pescatore de spugna (sommozzatore) che senza apparecchio si tuffa fino a 80 metri. Ann. de med. nav., Roma, 1915, i, 163–167.

Oliver, Sir T. An address on the physiology and pathology of work in compressed air. Brit. Med. Jour., London, 1909, i, 257–261.

PANUM. Untersuchungen über die physiologischen Wirkungen der comprimirten Luft. Pflüger's Archiv f. Physiol., Bonn, 1868, i, 125–165.

PHILIPPON, G. Action de l'oxygène et de l'air comprimé sur les animaux a sang chaud. Compt. rend. de l'Acad. des Sciences de Paris, 1893, cxvi.

——— Effets de la décompression brusque sur les animaux placés dans l'air comprimé. Compt. rend. de l'Acad. des Sciences de Paris, 1892, cxv, 186–188.

——— Effets produits sur les animaux par la compression et la décompression. Jour. de l'anat. et de physiol. norm. et pathol. de l'homme et des animaux, Publié par Duval, 1894, Nos. 3 et 4; 1895, No. 4.

PLESCH, J. Zur Prophylaxie und Therapie der Caissonkrankheit. Verhandl. d. deutsch. Kongr. f. innere med., Wiesbaden, 1910, xxvii, 254–263.

POL and WATTELLE. Mémoire sur les effets de la compression de l'air appliqués au creusement des puits à houille. Ann. d'hyg. pub. et de méd. lég., Seconde Série, 1854, i, 241–279.

REGNARD, P. La vie dans les eaux. Paris, 1891, G. Masson. V. Schr.

——— Recherches experimentales sur les conditions physiques de la vie dans les eaux. Paris, 1891, G. Masson.

——— Recherches experimentales sur l'influence des très hautes pressions sur les organismes vivants. Compt. rend. de l'Acad. des Sciences de Paris, xcviii, 745–747.

v. RENSELLAER. Pathology of caisson disease. New York Med. Record, 1891, xl, 141, 175.

——— Transactions of Med. Soc., New York and Phila., 1891, pp. 144–408.

——— Report of the Admiralty Committee on deep diving. Blue Book, London, 1907.

v. SCHROETTER. Der Sauerstoff in der Prophylaxie und Therapie der Luftdruckerkrankungen. Berl., 1906, A. Hirschwald.

v. SCHROETTER, H., HELLER, R., und MAGER, W. Zur Kenntniss der Todesursache von Pressluftarbeitern. Deutsche med. Wchnschr., 1897, Nr. 24, ff.

——— Experimentelle Untersuchungen über die Wirkung rascher Veränderungen des Luftdruckes auf den Organismus. Archiv. für die ges. Physiol., 1897, lxvii, 1–116.

——— Bemerkungen zu dem Aufsatze des Herrn Hofrath Dr. G. v. Liebig: "Warum man unter einem stark erhöhten Luftdrucke sowohl wie unter einem stark verminderten nicht mehr pfeifen kann." Munch. med. Wchnschr., 1897, Nr. 14.

SILBERSTERN, P. Die Gefahren der Caissonarbeit. Tr. XV Internat. Cong. Hyg. and Demogr., Wash. (1912), 1913, iii, 610–619.

SMITH, A. H. The physiological, pathological, and therapeutical effects of compressed air. Detroit, 1886. (A second edition of "The Effects of High Atmospheric Pressure, including the Caisson Disease," 1873.)

SMITH, J. L. The pathological effects due to increase of oxygen tension in the air breathed. Jour. Physiol., 1899, xxiv, 19.

SNELL, E. H. Compressed air illness. London, 1896.

THOMSON, T. K. An unsuspected cause of caisson disease. Tr. XV Internat. Cong. Hyg. and Demogr., Wash. (1912), 1913, iii, 608–10.

TRIGER. Mémoire sur un appareil et autres travaux, sous les eaux et dans les sables submergés. Compt. rend. de l'Acad. des Sci., 1841, xiii, 884–896.

TWORT, J. F., and HILL, L. Further experiments on the effect of breathing oxygen on the nitrogen dissolved in the urine. Proc. Physiol. Soc. Lond., 1911–12, 42–4.

——— Compressed air illness. I. Solubility of compressed air in water and oil. Proc. Physiol. Soc. Lond., 1910, xli, 5.

TWORT, J. F., WALTER, H. B., and HILL, L. Compressed air illness. II. The desaturation of the arterial blood as measured by the nitrogen dissolved in the urine. Proc. Physiol. Soc. Lond., 1910, xli, 6.

VERNON, H. M. The solubility of air in fats and its relation to caisson disease. Lancet, London, 1907, ii, 691–693.

——— The solubility of air in fats and its relation to caisson disease. Proc. Roy. Soc. Lond., 1907, Series B, lxxix, 366–371.

Conditions Due to Diminished Barometric Pressure

Air Service, Medical, War Department, Division of Military Aeronautics, Washington, D. C., 1919.

BARCROFT, J. The respiratory function of the blood. Cambridge, 1914.

——— Anoxemia. Lancet, London, Sept. 4, 1920, ccxix, No. 10, p. 485.

BARCROFT, J., COOK, A., HARTRIDGE, H., PARSONS, T. R., and PARSONS, W. Flow of oxygen through pulmonary epithelium. Jour. Physiol., Cambridge, 1920, liii, 450.

BERT, P. La Pression Barométrique. Paris, 1878.

BIRLEY, J. L. Principles of medical science as applied to military aviation. Lancet, London, 1920, cxcviii, Nos. 5048, 5049, 5050, pp. 1147, 1205, 1251.

CHRISTIANSEN, J., DOUGLAS, C. G., and HALDANE, J. S. The dissociation of O_2 from human blood. Jour. Physiol., London, 1913, xlvii, 2.

——— The absorption and dissociation of carbon dioxid by human blood. Jour. Physiol., London, 1914, xlviii, 244–271.

DOUGLAS, C. G., HALDANE, J. S., HENDERSON, Y., and SCHNEIDER, E. C. Physiological observations made on Pike's Peak, Colorado, with special reference to adaptation to low barometric pressures. Phil. Trans. Roy. Soc. London, 1913, Series B, cciii, 185 et seq.

DOUGLAS, C. G., HALDANE, J. S., and HALDANE, J. B. S. The laws of combination of hemoglobin with carbon monoxid and oxygen. Jour. Physiol., Cambridge, 1912, xlvi, 275.

DOUGLAS, C. G., and HALDANE, J. S. The causes of absorption of oxygen by the lungs. Jour. Physiol., Cambridge, 1912, xlvi, 305.

ELLIS, M. M. Respiratory volumes of men during short exposures to constant low oxygen tensions attained by rebreathing. Am. Jour. Physiol., Baltimore, 1919–20, l, 267.

GREGG, H. W., LUTZ, B. R., and SCHNEIDER, E. C. Compensatory reactions to low oxygen. Amer. Jour. Physiol., Baltimore, 1919–20, l, 302.

——— The changes in the content of hemoglobin and erythrocytes of the blood in man during short exposures to low oxygen. Amer. Jour. Physiol., Baltimore, 1919–20, l, 216.

HALDANE, J. S. Symptoms, causes and prevention of anoxemia. Brit. Med. Jour., London, 1919, No. 3055, p. 65.

HARTRIDGE, H. A. A spectroscopic method of estimating carbon monoxid. Jour. Physiol., Cambridge, 1912, xliv, 1–20.

——— The action of the various conditions on carbon monoxid hemoglobin. Jour. Physiol., Cambridge, 1912, xliv, 22–33.

KROGH, A., and KROGH, M. On the tensions of gases in the arterial blood. Skand. Arch. f. Physiol., 1910, xxiii, 179.

——— On the combination of hemoglobin with mixtures of oxygen and carbonic oxid. Skand. Arch. f. Physiol., 1910, xxiii, 217.

——— Some experiments on the invasion of oxygen and carbonic oxid into water. Skand. Arch. f. Physiol., 1910, xxiii, 224.

——— On the mechanism of gas exchange in the lungs. Skand. Arch. f. Physiol., 1910, xxiii, 235.

——— On the rate of diffusion of carbonic oxid into the lungs of man. Skand. Arch. f. Physiol., 1910, xxiii, 236.

LUTZ, B. R., and SCHNEIDER, E. C. The reactions of the cardiac and respiratory centers to changes in oxygen tension. Amer. Jour. Physiol., Baltimore, 1919–20, l, 327.

PETERS, R. A. Chemical nature of specific oxygen capacity in hemoglobin. Jour. Physiol., Cambridge, 1912, xliv, 131.

RAVENHILL, T. H. Some experiences with mountain sickness in the Andes. Jour. Trop. Med. and Hyg., London, 1912, xl, 313.

STADIE, W. C. The oxygen of the arterial and venous blood, etc. Jour. Exper. Med., New York, 1919, xxx, No. 3, p. 225.

v. TSCHUDI. Peru, Reiseskizzen aus den Jahren 1838–1842, ii, Saint Gallin, 1846.

ZUNTZ, LOEWY, MÜLLER, and CASPARI. Höhenklima und Bergwanderungen in ihrer Wirkung, etc. Berlin, 1906.

SECTION VI

DISEASES OF THE BONES AND JOINTS

CHAPTER I

DISEASES OF THE BONES AND JOINTS

BY ROBERT SOUTTER, M.D., F.A.C.S.

Diseases of the bones, p. 450:—Fractures, p. 450:—Fracture of the spine, p. 450; Fracture of the neck of the femur, p. 451; Fracture of the metatarsal bones, p. 451; Tibial tubercle injury or separation, p. 451.

Absence of bones, p. 452:—Congenital absence of the long bones—Absence of the fibula, p. 452; Congenital absence or partial absence of other long bones, p. 453; Absence and malformation of vertebræ, p. 454; Absence of ribs, p. 454.

Deformities, p. 455:—Deformity of the thorax, p. 455:—Supernumerary ribs—Absence of ribs, p. 455; Deformity of the chest from rickets, p. 455; Funnel chest, p. 455; Pigeon breast, p. 455—Deformity of the spine, p. 456:—Round shoulders—Stooped shoulders, p. 456; Scoliosis, p. 457; Spina bifida occulta, p. 458—Deformity of the toes, p. 459:—Claw-foot and hammer-toes, p. 459; Deformities of the fingers, p. 460:—Webbed fingers, p. 460; Hypertrophic osteoarthropathy, p. 461; Distorted fingers, p. 461—Other deformities, p. 461:—Congenital elevation of the scapula; Sprengel's deformity, p. 461; Bow-legs and knock-knees, p. 462; Acromegaly, p. 463; Achondroplasia (Chrondrodystrophia), Achondroplasia fetalis, p. 465.

Tuberculosis and other diseases of the bones, p. 465:—Tuberculosis of the bones and joints, p. 465; Tuberculosis of the spine (Pott's disease), p. 469; Periostitis, p. 476; Osteomyelitis, p. 477; Typhoid spine, p. 479; Infantile paralysis, p. 479.

Non-infectious paralyses, p. 482:—Cerebral spastic paralysis, p. 482; Spastic spinal paralysis, p. 483; Obstetrical paralysis, p. 484.

Other pathological conditions of the bones, p. 484:—Progressive muscular atrophy, p. 484:—Hand and forearm type (Aran-Duchenne), p. 484; Peroneal type, p. 484; Angel-wing type, p. 485; Large calf type, p. 485; Face and shoulder type (Landouzy-Déjerine), p. 485—Infantile scurvy, p. 485; Congenital torticollis, p. 485; Acquired torticollis, p. 486; Sciatic scoliosis, p. 487; Backstrain, p. 487; Osteogenesis imperfecta—Fragilitas ossium, p. 488; Osteomalacia, p. 488; Osteitis deformans (Paget's disease), p. 489; Painful heel—Bursitis, p. 489; Ingrown toe-nail, p. 490; Hallux rigidus, p. 490; Hallux valgus, p. 490; Hemophilic joint-swelling, p. 491.

Diseases of the joints, p. 492:—Dislocations, p. 492:—Congenital dislocation of the hip, p. 492; Snapping knee, p. 495; Congenital dislocation of the knee, p. 495; Congenital hyperextension of the knee,

p. 495; Congenital dislocation of the patella, p. 495; Traumatic dislocation of the patella, p. 496; Sacro-iliac injury, p. 496; Subluxation of the clavicle, p. 497; Congenital dislocation of the shoulder, p. 497; Chronic recurrent dislocation of the shoulder, p. 497; Recurrent dislocation of the patella, p. 497; Dislocation of the elbow, p. 498.

Tuberculosis of the joints, p. 498:—Tuberculosis of the hip, p. 498; Tuberculosis of the knee and ankle, p. 502; Synovial tuberculosis, p. 503; Rice bodies, p. 503; Tuberculosis of the shoulder, p. 503; Tuberculosis of the elbow, wrist and ankle, p. 503.

Arthritis of the joints, p. 505:—Arthritis, Osteo-arthritis, Arthritis deformans, p. 505; Degenerative or atrophic arthritis, p. 506; Proliferative or hypertrophic osteo-arthritis, p. 507; Infectious arthritis (non-tuberculous), p. 507; Acute arthritis in infancy, p. 508; Gonorrheal arthritis, p. 508.

Joint deformities, p. 510:—Deformities of the hip, p. 510:—Hip flexion, p. 510; Lordosis, p. 511—Coxa vara, p. 511; Coxa valga, p. 512—Deformity of the knee, p. 513:—Knee flexion, p. 513—Deformities of the ankle and feet, p. 514:—Postural conditions of the feet, p. 514; Equinovarus (club-foot)—Varus, p. 514; Pes cavus, p. 514; Equinus, p. 515; Equinovalgus—Valgus, p. 516; Flat-foot—Valgus, p. 516; Calcaneus—Calcaneovarus—Calcaneovalgus, p. 517; Flail-ankle, p. 517—Deformities of the wrist and hand, p. 518:—Madelung's deformity of the wrist, p. 518; Dupuytren's contraction, p. 518; Congenital club-hand, p. 518.

Other pathological conditions of the joints, p. 519:—Limited motion and deformity of the arms, p. 519; Ankylosis, p. 520; Semilunar cartilage displacement, p. 521; Prepatellar bursitis, p. 521; Loose bodies in the knee-joint (joint-mice), p. 521; Tenosynovitis, p. 521; Acute synovitis, p. 522; Intermittent synovitis with effusion, p. 522; Charcot's disease, p. 522; Gout, p. 522; Scapula crepitus, p. 523; Sprained ankle, p. 524; Subdeltoid bursitis, p. 525; Ischemic paralysis (contraction), p. 525.

DISEASES OF THE BONES

FRACTURES

Fracture of the Spine.—If there is no immediate crushing of the cord, fracture may simulate disease and may not be differentiated at first, except by the history of trauma. If there is marked crushing of the vertebræ, there may be deformity. The *x*-ray is an aid in diagnosis. Pain and tenderness are usually present, and more or less disability, depending upon the injury. Pressure symptoms develop sooner or later if the spine buckles, or due to congestion following the injury. If the cord is crushed, there will be shock, paralysis, both sensory and motor, below that level, and paralysis of the bladder and rectum. The reflexes may be increased or lost, depending upon the severity of the trauma.

A crushed vertebra or two will sometimes disintegrate progressively so that the symptoms of pressure develop gradually. The deformity will increase as the bone disintegrates.

TREATMENT.—The treatment is by support and **fixation,** or **correction** of the **deformity** by recumbency on a frame, followed by apparatus. **A bone-graft** is often necessary to prevent the recurrence of pressure symptoms, or to prevent the recurrence of deformity after severe fractures or crushing of the vertebræ. The results are very satisfactory. Bone-grafting should be done only by those thoroughly familiar with the technic and with the best methods of asepsis.

The prognosis is good in these cases.

Fracture of the Neck of the Femur (*Recent*).—SYMPTOMATOLOGY.—The symptoms are pain, local tenderness, possibly crepitus and deformity. The pain is often referred to the knee. Usually there is pain in the groin or near the hip-joint if the surgeon strikes the patient's heel with his hand. An *x*-ray plate will show the fracture. There is a history of a fall or of some other injury.

TREATMENT.—The leg should be disturbed as little as possible until all apparatus is ready. Then, under anesthesia, **traction** is applied, and the surgeon **presses** on the **trochanter** until a position of extreme abduction and hyperextension, recommended by Whitman, is reached. The amount of abduction and hyperextension necessary should be determined by trying out the good leg. With the leg in this position, a well-fitting **plaster of Paris bandage** is applied to the thorax, pelvis (including the tuberosity of the ischium), thigh, leg and foot. The patient is placed on a Bradford frame. The leg below the upper third of the femur is unsupported by the bed. The patient may be allowed to use a bed-rest in two weeks—his health will not permit the recumbent position longer than that. This fracture tends to occur in the aged, who cannot endure prolonged recumbency well.

Fracture of the Metatarsal Bones.—SYMPTOMATOLOGY.—The symptoms are pain, tenderness and swelling. The pain is not always excessive. Patients may walk for six months or more without treatment. Pain is constantly present to a slight degree, and will persist until the bone is united.

The cause may be very slight. An *x*-ray examination is sometimes necessary for diagnosis.

TREATMENT.—Treatment consists in **immobilization** of the foot and ankle for five weeks by a **plantar splint** and an **ankle and foot plaster.** Walking on the foot is allowed after five weeks, if the bone has united and the swelling has subsided. The plaster must be kept in place when the patient first begins to walk. If the bone does not unite in three months an **operation** will be necessary.

Tibial Tubercle Injury or Separation.—The epiphysis of the tibial tubercle is united about the eighteenth year and may be separated by trauma or by sudden contraction of the extensor muscles of the thigh. There is pain, swelling and local tenderness. In extreme cases there is disability and weakness. An *x*-ray examination will show the separation.

TREATMENT.—Treatment consists in **fixation in extension** long enough to allow the bone to unite. Occasionally an **operation** is necessary to unite the separated bone. The condition is not a serious one.

ABSENCE OF BONES

Congenital Absence of the Long Bones.—Absence of the Fibula.— The absence or partial absence of the fibula or of one of the other long bones is not uncommonly seen in an orthopedic clinic. This condition varies from a partial to a total absence of the fibula (Fig. 1). In some instances, only the epiphyseal line, or growing portion of the bone, is affected, without any apparent absence of the bone. In this type of case, the structures of the leg do not grow as they should, and as a result there are deformities in the position of the foot or in the line of the leg

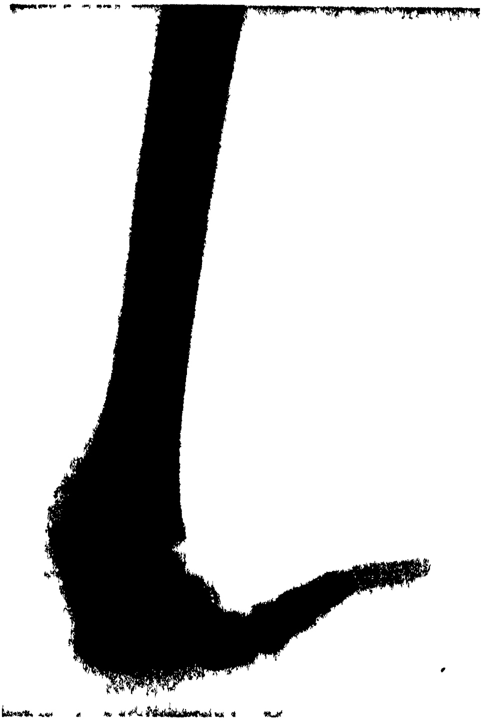


FIG 1—CONGENITAL ABSENCE OF THE FIBULA AND DEFORMITY OF THE FOOT

TREATMENT.—**Operations** are performed to correct the deformity or to supply the bone when absent. In very slight cases an osteotomy of bone is all that is necessary to allow correction of the deformity. In other cases, the bone must be cut through with an osteotome, the gap separated and filled by an **inlay graft.** The inlay graft is usually preferable to the medullary graft in this type of case. For a total absence of the fibula, a bone-graft may be placed beside the tibia, or a graft may be implanted into the lower tibia and into the tarsal bones to give support to the ankle.

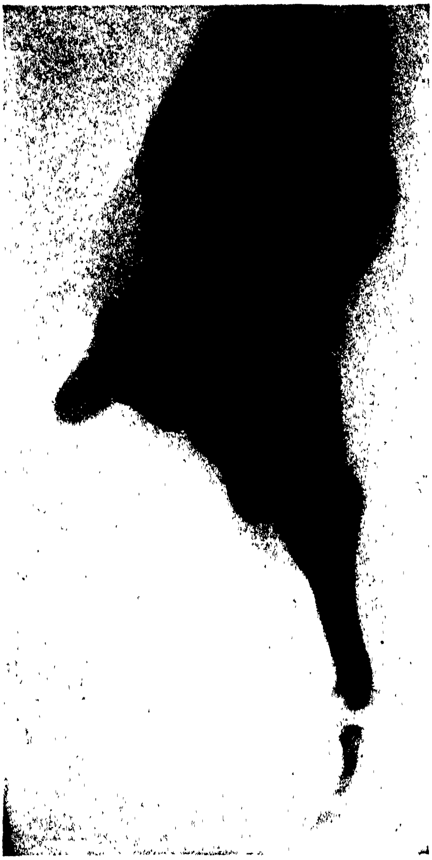


FIG. 2.—CONGENITAL ABSENCE OF METATARSALS AND TOES.

Congenital Absence or Partial Absence of Other Long Bones.—In partial absence of other long bones, the condition is very much the same as in absence of the fibula, and may vary from a defect in the epiphyseal line to a partial or total absence of the bone. When the humerus or the femur are defective, the bones below are often shortened or deformed; but when the bones below are present there is usually some small bone corresponding to the "absent" ones. In the hand or foot any bone may be absent beyond the carpus or tarsus; or it may be affected as above described. If one or more carpal or tarsal bones are

absent, the metacarpal or metatarsal beyond it are apt to be missing (Fig. 2).

Absence and Malformation of Vertebræ.—There may be absence of vertebræ without any additional sign other than an obvious shortness of that part of the spine. Often there is a cleft in the spinal column at the point of deficiency. Supernumerary or deformed vertebræ may cause deformity of the spine; this condition is also one of the causes of congenital scoliosis.

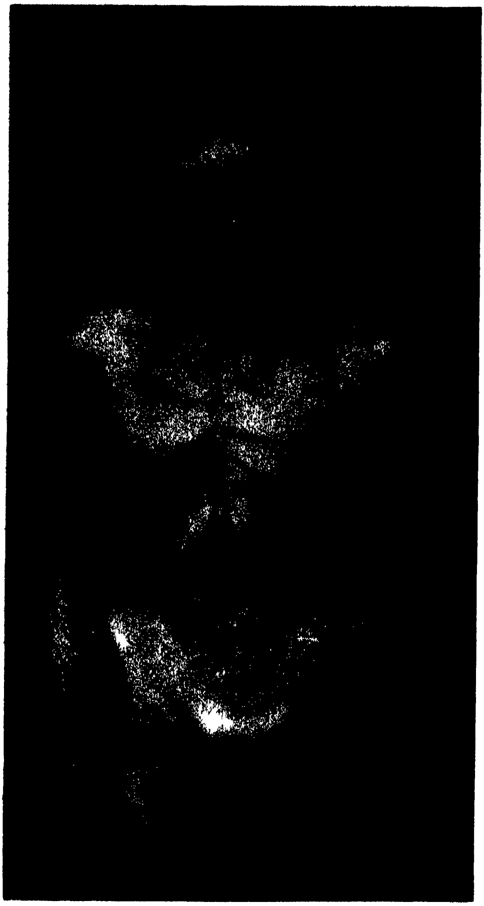


Fig 3 —Supernumerary Rib.

Treatment —The cases should be treated for the scoliosis deformity, the **spine straightened** as much as possible and the **muscles developed** to maintain the correction.

Absence of Ribs.—This condition is not uncommon. When it is present there is apt to be unequal, defective formation of the muscles. This may lead to deformity of the spine, and to asymmetry of the thorax.

DEFORMITIES

Deformity of the Thorax

Supernumerary Ribs—Absence of Ribs.—There may be supernumerary ribs or absence of ribs, either in the upper or lower part of the chest. The condition may be unilateral or bilateral. Either a single rib or many ribs may be absent. In some instances, supernumerary ribs cause pain, according to certain authors. In some instances this is due to other causes which would occasion the same pain in the case of patients without cervical ribs. Nevertheless, the pain is often attributed to the supernumerary ribs. If the cervical rib is unilateral, the spine may develop a lateral curvature, as such a rib is often connected with a defective supernumerary vertebra (Fig. 3).

Deformity of the Chest from Rickets.—In rickets, the ribs and cartilages are softer than normal. In breathing, the action of the diaphragm and muscles sucks in the ribs or their cartilages and causes various deformities. In rachitic children the rounding of the soft spine will increase the deformity of the chest. This may cause a symmetrical deformity or an asymmetrical development of the thorax, or a sagging more to one side than to the other. These deformities are due to a soft condition of the bone affecting the growth and development of the chest.

Funnel Chest.—In funnel chest there is a hollow deformity over the various parts of the sternum. Some authors have attributed the condition to a defective ossification or to pressure of the chin on the thorax before birth.

Pigeon Breast.—Pigeon breast is a deformity characterized by an undue prominence of the sternum and of the cartilages of the ribs. This is usually in the median line but may be unilateral.

CAUSATIVE FACTORS.—The cause is usually rickets. There is an increase in the anterior, and a decrease in the lateral diameter.

Deformities of the thorax are also due to a malposition of the spine; or they may be due to asymmetry or lack of development of one or more vertebræ, to disease of the spine, to asymmetry of the pelvis, to a difference in the length of the legs, to asymmetrical development of the muscles, or to disease of the respiratory organs—pneumonia, empyema, pyopneumothorax, etc.

TREATMENT.—Deformities of the thorax are treated by **correction apparatus** on which the patient rests. These are used together with **braces** and **exercises**, to expand the chest. The Clapp crawling exercises are often very useful in this type of deformity. In small children braces should be avoided as much as possible.

Deformity of the Spine

Round Shoulders—Stooped Shoulders.—Etiology.—Round shoulder is a posture of relaxation, weakness and fatigue. Faulty attitudes in standing and sitting are the common causes (Fig. 4). It is to be found also in the case of those who, through occupation or otherwise, carry heavy loads on their backs. Tight, long garters, and waists that hang from the tip of the shoulders favor round and drooping shoulders (Fig. 5). No less serious as a causative factor is an overheated house, and an indoor life with an atmosphere of indolence, limitation and tension. School life tends to produce round back by its confinement to the desk. The mental element is often of importance.

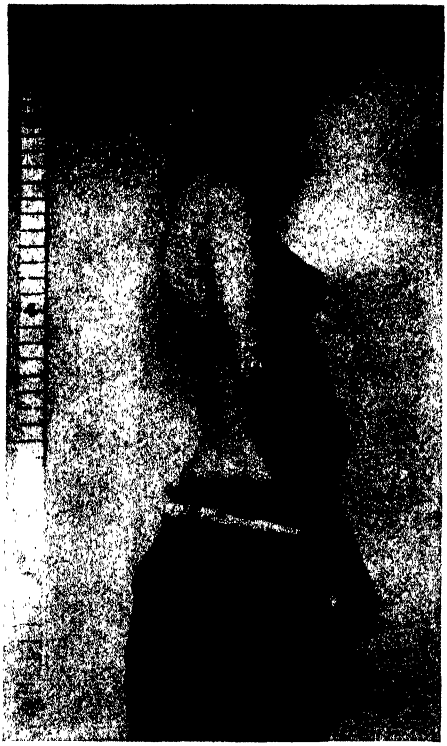


Fig. 4.—Faulty Attitude in Standing. Round Back.

Symptomatology.—The most striking symptom is an increase in the dorsal physiological curve. Pain may occasionally be present.

TREATMENT.—Treatment consists of favorable surroundings, **correction of faulty attitude** and **proper dress**. These may be supplemented by **exercises** and **apparatus**.

Scoliosis.—ETIOLOGY.—Postural scoliosis is due to overloading the spine or to a decreased resistance in growing individuals who sit, stand or work in faulty and onesided postures. Some forms of astigmatism and asymmetrical weakness of the eye-muscle may lead to faulty posture. Unilateral deafness may also serve to favor the development of scoliosis. The condition may also be caused by empyema, contractures from disease, trauma, defective ribs or vertebræ, difference in the length of the legs, and asymmetrical pelvis (Figs. 6 to 10).

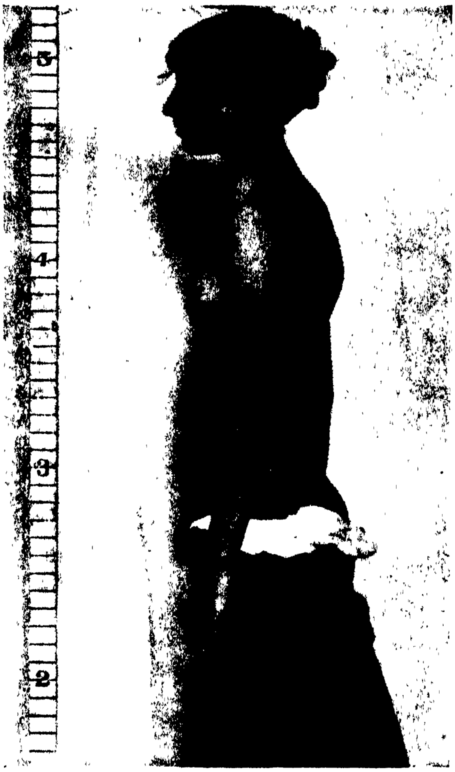


FIG. 5.—ROUND SHOULDERS.

SYMPTOMATOLOGY.—There is an evident, slight or extreme curve in the spine, with or without prominence of the ribs on one side (rotation). Many digestive disturbances and visceral disorders are due to habitual faulty attitudes. In certain cases there may be compression of the thoracic viscera, causing shortness of breath and rapid pulse.

Treatment.—Slight cases are improved by corrective **exercises, light braces** and corrective **apparatus.** Extreme cases may be improved by gradual or forcible correction in **plaster of Paris.** The physician should adapt the method of treatment to the patient. Delicate children and adults who are sickly should be treated by the gentler corrective methods at first. These consist in braces, developing exercises and gymnastics. Plaster of Paris should be reserved until they are stronger, and, when used, should be supplemented and followed by healthful exercises.

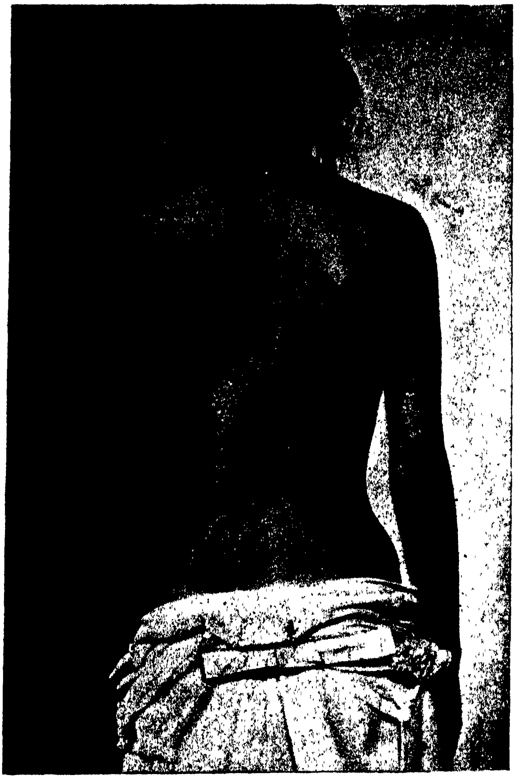


Fig. 6.—Scoliosis, Showing a Double Curve.

Spina Bifida Occulta.—From the orthopedic point of view, spina bifida is of interest because of the muscular weakness or paralysis and because of the deformity of the spine, which may consist in a postural curve or in an extensive scoliosis with bony changes. There may be club-feet or club-hands, deformed or dislocated hips, subluxated or contracted knees, various malformations, or complete or partial absence of bones. Trophic ulcers are not uncommon. The deformities may be of congenital origin or due to paralysis or static conditions, and there may be incontinence of feces and urine. Some cases of spina bifida show only a few of the above deformities—in others they are all present.

Treatment.—Each deformity will require separate treatment. The muscular weakness will require **muscle-training**, **exercise** and **massage**. **Braces** are useful in correcting deformity and as an aid in locomotion. The **tumor,** when not too large, may be left for years untreated and then **removed,** the sac membrane being sometimes inverted, with comparative safety, without being opened.

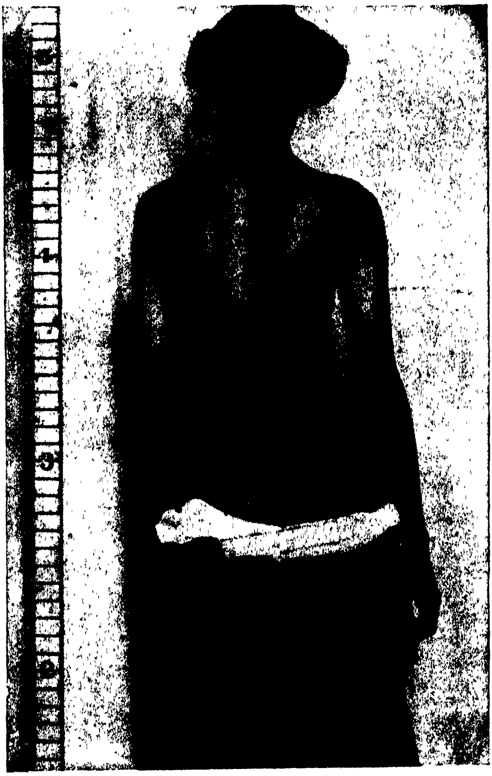


Fig. 7.—Scoliosis, Showing Total Curve.

Deformity of the Toes

Claw-foot and Hammer-toes.—This condition consists in contraction of one or more of the toes. It may be bilateral, and either congenital or acquired. The second phalanx is flexed while the third is extended (Fig. 11).

Treatment.—The flexed position of the toes, when slight, may be corrected by **tenotomies** of the capsule and tendons maintaining the deformity. In extreme cases an **operation** on the bone is necessary. The heads of the metatarsals should not be cut or removed. When a bone operation is necessary, it should be on the bone of the phalanx (Fig. 12).

Deformities of the Fingers

Webbed Fingers.—Two or more fingers may be webbed to a varying length by skin, fibrous tissue or even by muscle and bony tissue (Figs. 13 and 14). The thumb is seldom involved. The fingers are sometimes united at their tips in pairs or in a mass.

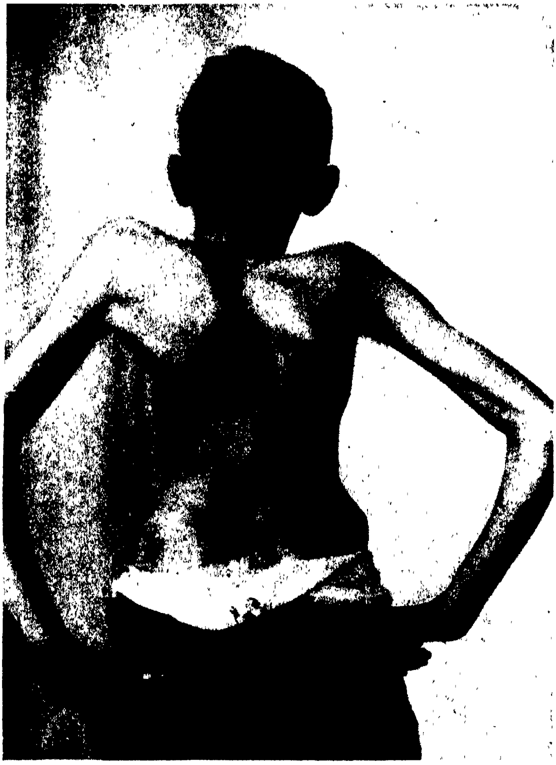


Fig. 8.—Scoliosis with Rotation.

Treatment.—The fingers can usually be separated by a **plastic operation.** The skin from the back of one finger is incised in such a way as to be carried with the second finger, covering its front and side, while the skin from the front of the second finger is incised in such a way that it is carried away with the first finger when they are separated, and covers its side and back. In this way no granulating area is left.

Hypertrophic Osteo-arthropathy.—This condition usually accompanies preëxisting chronic pulmonary disease. There is marked clubbing of the fingers, overgrowth of the nails, new bone deposit in the metatarsal and metacarpal phalanges and in the distal extremities of the adjoining bones of the arms and legs.

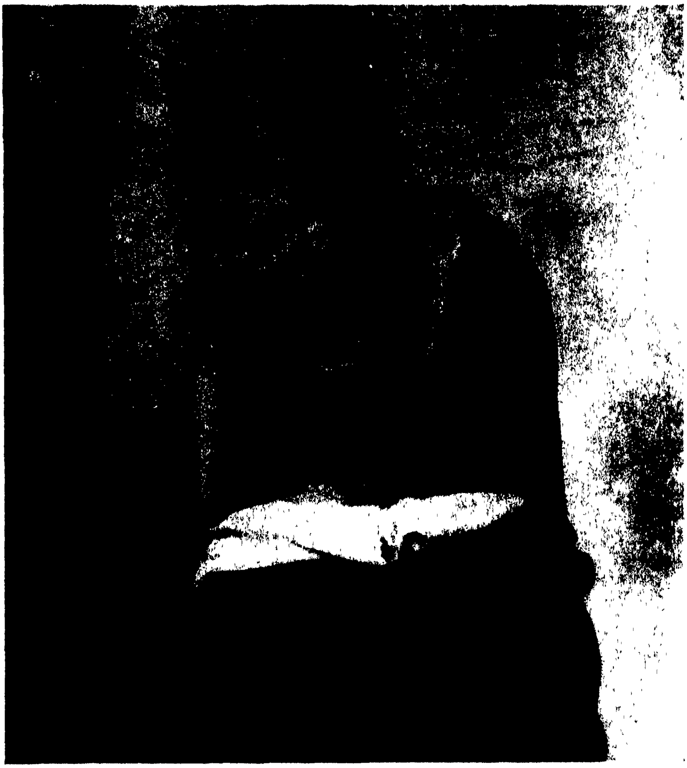


FIG. 9.—SCOLIOSIS. Showing rotation when patient leans forward.

Distorted Fingers.—This condition is congenital, and not uncommon. It should be treated as early as possible by **manipulation, exercise** and **apparatus,** or by **plastic operations.**

Other Deformities

Congenital Elevation of the Scapula—Sprengel's Deformity.—This condition may affect one or both scapulæ. The scapula is held high and is usually inclined forward and outward as well as upward and forward. It is less movable than normally on account of the shortening of the muscles and of one or more fibrous or bony bands which attach it to the spine or to the ribs. The position of the scapula causes deformity of the neck and scoliosis or a flat chest anteriorly (Fig. 15).

TREATMENT.—The asymmetry and scoliosis should be treated by stretching and development **exercises** and **gymnastics**, **braces**, etc. Very often it is necessary to **remove the bands by operation** and draw the scapula down to the normal position. The operation should be followed by exercises to overcome the deformities of the spine and chest and to promote the normal mobility of the scapula.

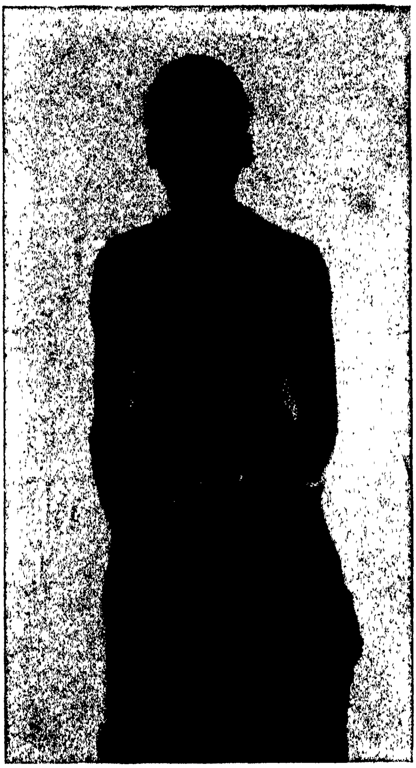


FIG. 10.—SCOLIOSIS. Right dorsal, left lumbar curves.

Bow-legs and Knock-knees.—In bow-legs the bowing may be of the femur and tibia or of the tibia alone (Fig. 16). It is a rachitic deformity of children. Knock-knee is an internal prominence of the knee. The bones of the leg form an angle with the femur. The knees are approximated, and the feet are held apart on standing.

TREATMENT.—The deformity is easily corrected by a linear **osteotomy** at the point of greatest curve, and then the leg is held in a slightly

overcorrected position until locomotion is established. Extreme deformities are very satisfactorily treated in this way. In anterior bowing of the tibia, a small **wedge of bone** is removed instead of a linear osteotomy being performed, which is sufficient elsewhere but not in this case.

When a deformity is due to rickets (Figs. 17 to 19) the bones should **not be operated** upon if the epiphyseal line appears irregular and undefined in the *x*-ray plate. If the bones are hard and the patient is three or four years old at least, and the *x*-ray examination shows a clearly defined line, an operation may be advisable. In young children, when the bones are soft, **braces** are usually satisfactory as a means of correcting the deformity, if the curve is near the middle of one of the long bones. In children over five it is better to operate as a brace will accomplish little, and the strain on the joint is sometimes considerable.

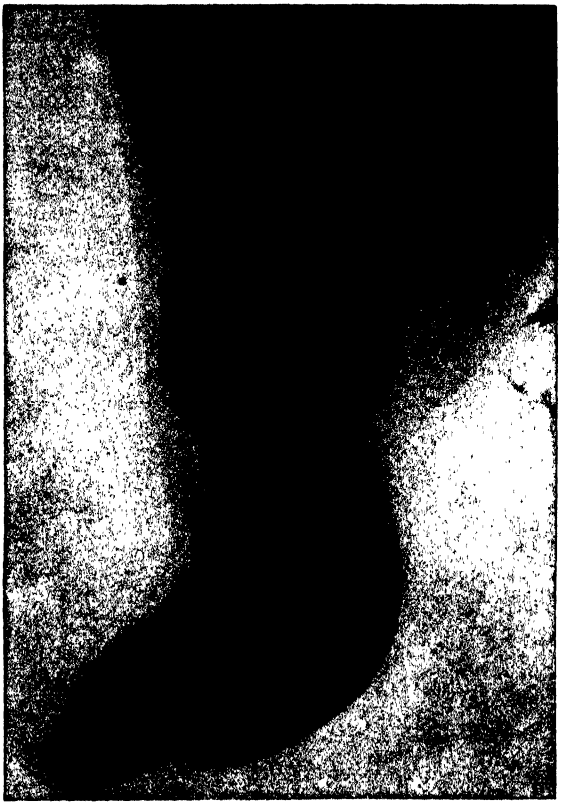


FIG. 11.—HUMPED FOOT AND CLAW-FOOT.

Acromegaly.—In acromegaly the jaw, hands and feet or the fingers or toes, or all of these extremities, may enlarge. The changes may be

FIG. 12.—SUPERNUMERARY FOOT.

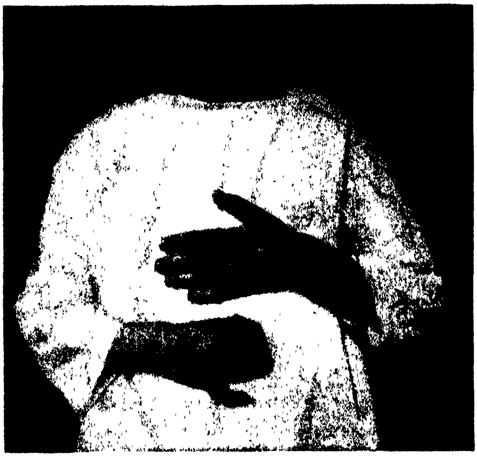


FIG. 13.—CONGENITAL DEFORMITY OF FINGERS, AND WEBBED FINGERS.

slight and take place slowly over a long period of time, diminishing after the patient is fifty years of age. There is a chronic form with marked enlargement of the head, hands and feet lasting from eight to thirty years. A malignant form is also found which progresses rapidly and lasts about three years. In this form there is general atrophy, cachexia, cardiac disturbance and death. It is supposed to be due to disease of the pituitary gland and analogous to myxedema with disease of the thyroid gland.

Achondroplasia—(Chondrodystrophia)—Achondroplasia Fetalis.—In this condition the shafts of the long bones of the arms and legs grow small. The end of the bones at the epiphysis grows and broadens. The wrists, ankles, and knees enlarge and broaden. The body and head grow; the patient is a dwarf with short legs and short arms, and a large head and body (Figs. 20 to 22). The condition differs from rickets in that there is very slight proliferation of cartilage.

FIG. 14.—WEBBED TOES.

Tuberculosis and Other Disease of the Bones

Tuberculosis of the Bones and Joints.—ETIOLOGY.—Tuberculosis of the bones and joints is due to an infection by the tubercle bacillus. The modes of entrance is probably through the mouth, the bronchial glands or the glands of the intestine, and thence to the bone. The disease may occur at any age, but it is most common in children. There is often a history of trauma. The various joints are attacked in the following order of frequency: spine, hip, knee, ankle and elbow.

SYMPTOMATOLOGY.—Tuberculosis of the bones and joints is characterized by atrophy, slow progression of the disease and comparatively little pain. At times the pain may be very severe, but in observing the disease over a long period of time pain is not found to be a prominent symptom. Local atrophy is marked. With the *x*-ray the atrophy of the bone may be noticed.

The limitation of motion at the joint is due at first to spasm, later to the changes about the joint. As these changes improve the joint may become movable again. When there is abscess formation following tuberculosis of the bone there may be pain due to the tension of the abscess. The pain diminishes as the soft tissues give way and the tension is diminished.

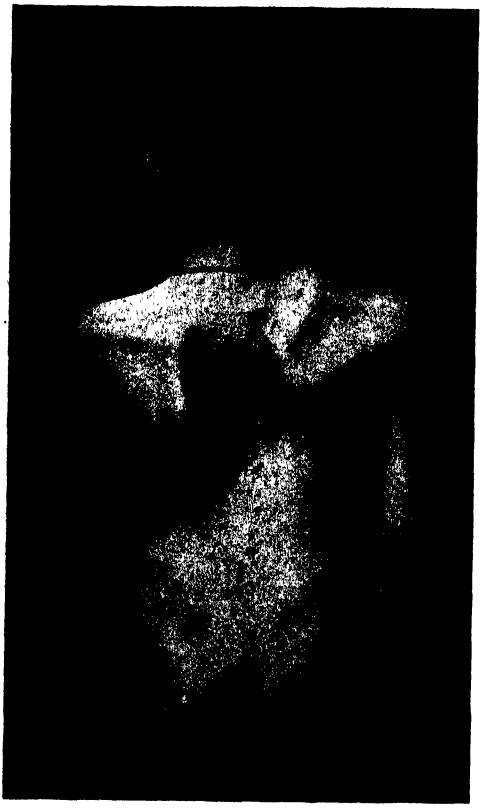


Fig. 15.—Congenital Elevation of the Scapula.

The general symptoms in tuberculosis of the bone come on gradually. The disease has usually progressed for some time before the constitutional symptoms are marked. When the proper treatment is introduced the general symptoms improve markedly. Usually there is an appearance of good general health.

Treatment.—In the treatment of tuberculosis, general hygienic measures are very important. Locally the disease should be treated by

rest, immobilization and **protection from jar.** The efficiency of the treatment may be judged by the local comfort and the general constitutional improvement. The local improvement is gradual.

Operation in tuberculosis of the bones is to be **avoided.** The abscess should not be opened, as it will usually absorb, even when very large. Should the pain be excessive or the constitutional symptoms grow markedly worse, it may be necessary to **open** a tuberculous **abscess.** In these instances, the abscess cavity should be opened by large incisions and thoroughly wiped out with gauze. Drains are placed and the incisions gaped as wide as possible. In the after-treatment no injections or irrigations should be used. Where a careful Carrel-Dakin technic has been carried out in tuberculosis of the bone, the results have not been as satisfactory as in ordinary bone-abscess.

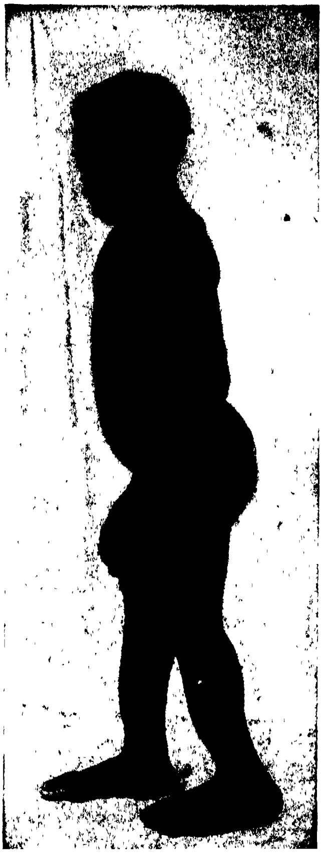


FIG. 16.—RACHITIC DEFORMITY. Anterior bowing of the tibiæ.

PROGNOSIS.—In the majority of cases treated early the outlook is favorable. Much depends upon the surroundings of the patient, upon the general condition of the patient, and upon the power of resistance against the tubercle bacilli. If these conditions are satisfactory the prognosis is very favorable.

PATHOLOGY.—Tuberculosis of the bones and joints usually begins in the spongy tissue of the epiphysis, or in the juxta-epiphyseal and adjacent region. After the stage of tuberculosis infiltration the process takes one of three forms—namely, the infiltration absorbs, breaks through the periosteum and discharges, or produces an arthritis. "Cold" abscess may be formed about the joint. The contents of the abscess may be quite thick or else watery. Tubercle bacilli may be found, but pyogenic organisms are absent. Repair takes place by the formation of fibrous tissue. Cartilage or bone may be laid down in the process of repair. An x-ray examination, when the disease has progressed sufficiently, will show a small focus in the bone, marked atrophy in the bone, and a decrease in the size of the cortex as compared with that on the unaffected side.

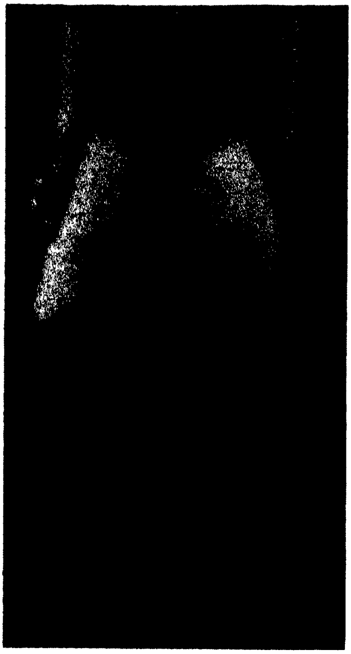


FIG. 17.—BOW-LEGS DUE TO RACHITIS.

Tuberculosis of the Spine (Pott's Disease).—This condition is characterized by more or less destruction of the bodies of the vertebræ, the process being slow (Fig. 23). As the bodies are progressively destroyed a marked kyphosis is formed (Figs. 24 and 25). With the increase of the kyphosis, pressure symptoms on the cord may be noted, even to the point of destruction.

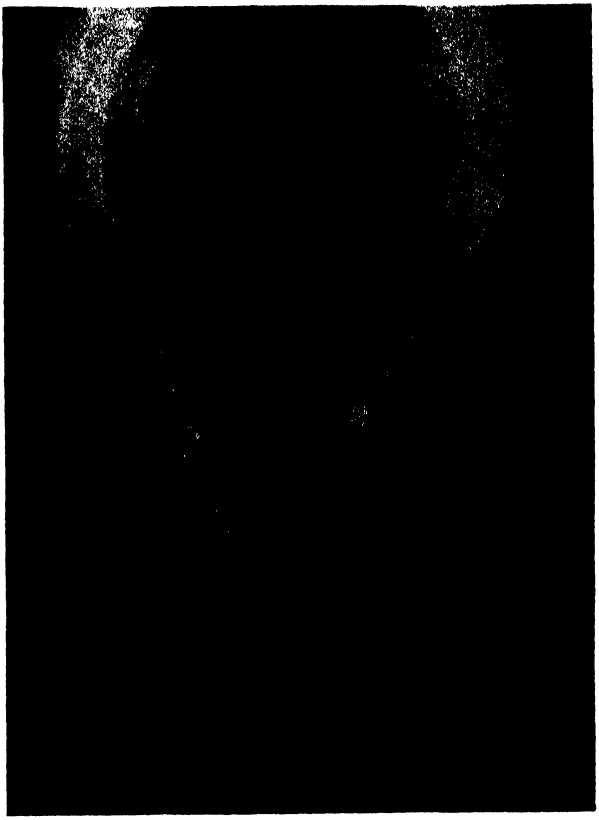


FIG. 18.—RACHITIC DEFORMITIES. *X*-ray.

ETIOLOGY.—Tuberculosis of the spine is a disease which attacks male and female alike. Any of the vertebræ may be involved. A generally lowered resistance is the predisposing cause, while a jar or blow may be the localizing cause.

SYMPTOMATOLOGY.—In the untreated cases there is often a marked decline in the general condition of the patient, with loss of flesh. Very often, however, this is not noticed early in the disease. The patient carries the spine carefully, stoops cautiously in picking up articles from the floor, and in sitting will often use his hands to steady the spine by leaning as he sits, lifting the weight of the shoulders or the weight of the head with his hands. Very often the patient will complain of abdominal or chest pain, due to congestion or pressure on the nerves coming from the spinal canal. Sleep is often disturbed suddenly at night by bad dreams or, in children, by night cries. The patellar or other reflexes are usually increased. There is a marked muscle-spasm in the region of the disease. With tuberculosis in the cervical region

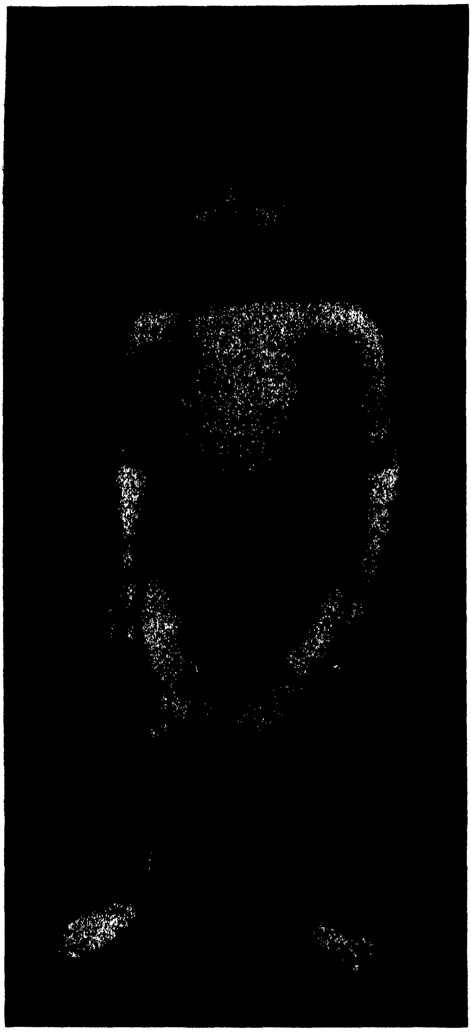


FIG. 19.—KNOCK-KNEE DUE TO RACHITIS.

there may be a slight torticollis accompanying the spasm of the cervical muscles (Fig. 26). In the dorsal region the spine is held rigidly by the muscles. In the lumbar region there is more or less psoas contracture, depending upon the severity of the condition, with a limitation of the hyperextension of the leg. As the disease progresses a large or small knuckle is formed, depending upon the number of vertebræ involved, and the amount of destruction of the bodies on the vertebræ.

FIG. 20.—ACHONDROPLASIA.

As the spine bends backwards there is more or less compression of the cord, increasing the reflexes, especially the knee-jerks, and the psoas spasm, and, when extreme, causing ankle-clonus. Abscesses occur in tuberculosis of the spine, as in tuberculosis of the joints. Abscess in cervical Pott's disease may appear as a deep cervical abscess or as a retropharyngeal abscess. In the dorsal region it may appear on one side of the spine or may extend into the mediastinum, causing pain, cough and dyspnea, or it may rupture into the lung. In the lumbar region it appears as a psoas abscess. If the disease has progressed sufficiently the *x*-ray examination will show a focus in the body or an anteroposterior flattening of the body. The intervertebral disk may be obliterated or destroyed and the process may be shown to involve several vertebræ.

Differential Diagnosis.—In the cervical region, tuberculosis of the spine may be differentiated from *congenital torticollis* by the following characteristics of the latter ailment: facial asymmetry, the uneven pull of the muscles, the freedom from pain, the lack of general constitutional symptoms, the absence of neuralgic pain, the absence of characteristic attitude and the support of the head with the hands, and the absence of thickening of the tissues at the site of the disease. The presence of an abscess will often settle the diagnosis as far as torticollis is concerned. It must not be forgotten, however, that irritations of the scalp, or disease of the tissue or tonsils often cause enlargement and irritation of the cervical lymph-glands, simulating disease of the spine. Ear conditions may be differentiated by the local examination, the tenderness about the mastoid being diagnostic.

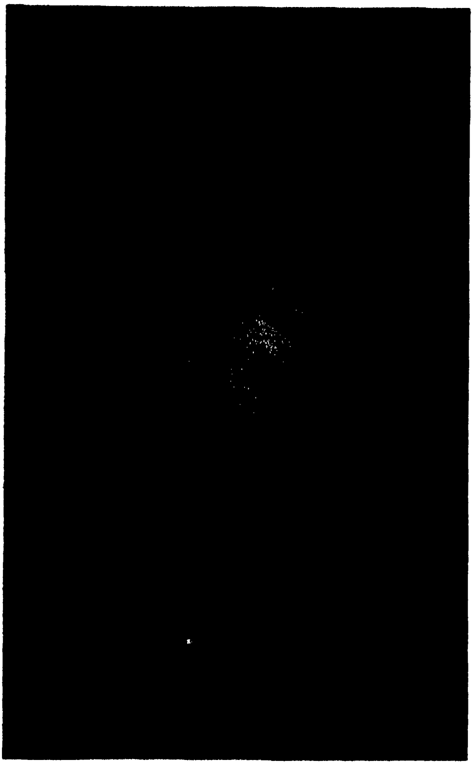


Fig. 21.—Achondroplasia, Showing Flattening of the Vertebræ.

In *meningitis* the disease generally begins abruptly with a chill. Vomiting, headache, excruciating pain, and Kernig's sign are almost always present; delirium is rarely absent; there is extreme cutaneous hyperesthesia and nystagmus, a temperature of from 101° to 103° F. (38.33° to 39.44° C.), and usually leukocytosis. Tuberculous meningitis sometimes follows tuberculosis of the bones in the spine and elsewhere; its onset is usually very gradual. *Traumatic conditions* of the spine, with symptoms developing long after the injury, are sometimes difficult to differentiate from tuberculosis of the vertebræ, but the recovery under treatment will not take as long as in Pott's disease. In certain cases it is necessary to give protective treatment before a certain diagnosis can be made.

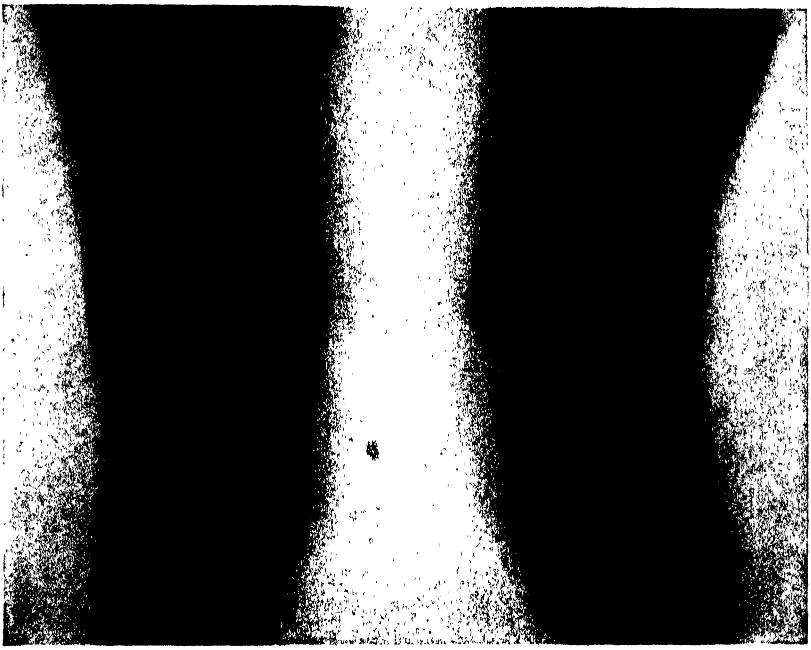


FIG. 22.—ACHONDROPLASIA. *X*-ray of the knee.

In *rheumatism* the onset is usually sudden, and under proper treatment the symptoms will subside. The kyphos may be very marked in the dorsal and lumbar spine in tuberculosis.

TREATMENT.—*General Treatment.*—The early treatment should be **recumbency** in a posterior **plaster shell, hyperextended** at the point of the knuckle. This separates the bodies of the vertebræ at the points of disease and allows the proper rest and repair. The hyperextension is gradually increased. The treatment need not be painful. When the local symptoms have subsided, if the reflexes are not exaggerated a well-fitting **brace** or **plaster of Paris jacket** should be used until the disease is completely cured. In cases in which the deformity is marked recumbent treatment should be introduced to correct the deformity. The Pittsburg frame which hyperextends the knuckle freely or the gradual increase of hyperextension in the plaster shell will almost entirely overcome the deformity in most cases. Where paralysis is beginning or has existed for any length of time, the recumbent position on a hyperextended posterior plaster is the best treatment. The extent of the kyphosis, and any change in it, should be measured. This can be done by fitting a strip of sheet lead to the contour of the kyphos and then making a tracing on cardboard. The accuracy of the tracing should be tested by fitting the cardboard to the kyphos. Once this is obtained, any change in the kyphos can be readily detected.

FIG. 23.—TUBERCULOSIS OF THE SPINE. Note the destruction of the bodies of the vertebræ.

Plastic Operations for Fixation of the Spine.—Operations for fixation of the spine in the region of the disease have been used with a good deal of success. At the Children's Hospital in Boston and in general orthopedic practice, the operation is not done on children, as a rule, unless the deformity is increasing, or where the best possible care is not available at home. There are some exceptions to this rule.

In adults, however, the operation is distinctly advisable if performed by experienced clinicians, as it usually shortens the convalescence by from three to five years. The spine should be immobilized above and below as well as in the region of the kyphos. Careful technic is very important. Dr. Hibb's operation is performed by **bending down the spinous process** in one line, forming with the periosteum a bony ankylosis in the region of the kyphos. Dr. Albee's operation consists in removing a long **graft** from the tibia and placing it between the split spinous processes. When performed by a surgeon thoroughly familiar with the technic, these operations are extremely valuable. It must be remembered, however, that these operations fix the spine, but

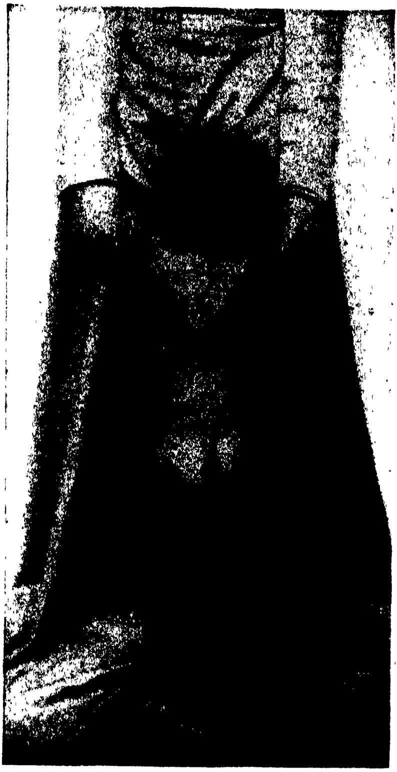
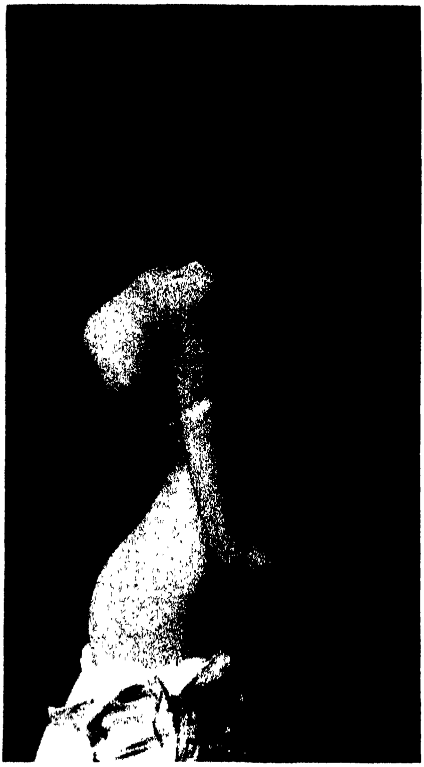



FIG. 24.—TUBERCULOSIS OF THE SPINE WITH SMALL KYPHOS.

FIG. 25.—TUBERCULOSIS OF THE SPINE. Neglected case, large kyphos.

by fixing the spine help to cure the disease. The patient must still **take** care of his general health and of his spine until he is entirely well. In recovering from Pott's disease the **general health** and activity should be **carefully guarded**. The improvement of the general health and local symptoms goes hand in hand with the local cure. Tuberculosis of the spine is distinctly amenable to treatment. Disease at any one level should be treated by fixation by apparatus holding the pelvis, dorsal and lumbar spine. Where the disease is above the sixth dorsal vertebræ, the cervical spine should be held.

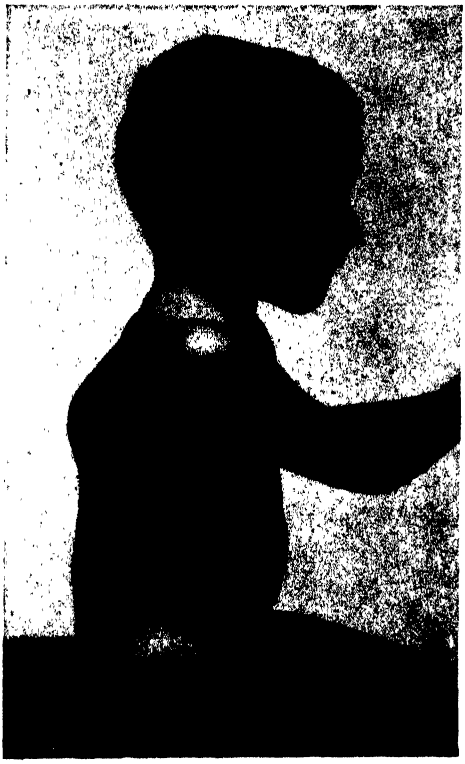


FIG. 26.—TUBERCULOSIS OF THE SPINE. Note the marked kyphosis.

PATHOLOGY.—See Tuberculosis of the Bones and Joints.

Periostitis.—Periostitis is an infectious condition of the periosteum. In syphilitic periostitis the periosteum may be stripped and elevated, the whole process being painless. A periostitis due to pyogenic bacteria rarely occurs without some infection of the bone below, and for that reason it may be considered with that condition.

Osteomyelitis.—ETIOLOGY.—Osteomyelitis is usually produced by the pyogenic bacteria. Occasionally the pneumococcus or the typhoid bacillus may cause the process. The femur, the tibia and the humerus are the bones most commonly affected (Fig. 27).

SYMPTOMATOLOGY.—The symptoms may be mild and the pain slight or very severe, with sudden onset, high temperature extending to 106° F. (41.11° C.), great pain, swelling, tenderness, local heat, redness or surface edema, the appearance of grave illness, delirium resembling a typhoid condition and a greatly increased white-cell count. The virulence varies, the process is destructive, the bone is destroyed, sequestræ form, and the pus extends up and down the bony canal and strips the periosteum from the bone. If the disease is near or involves the epiphysis, the growth of the bone will be seriously impaired.

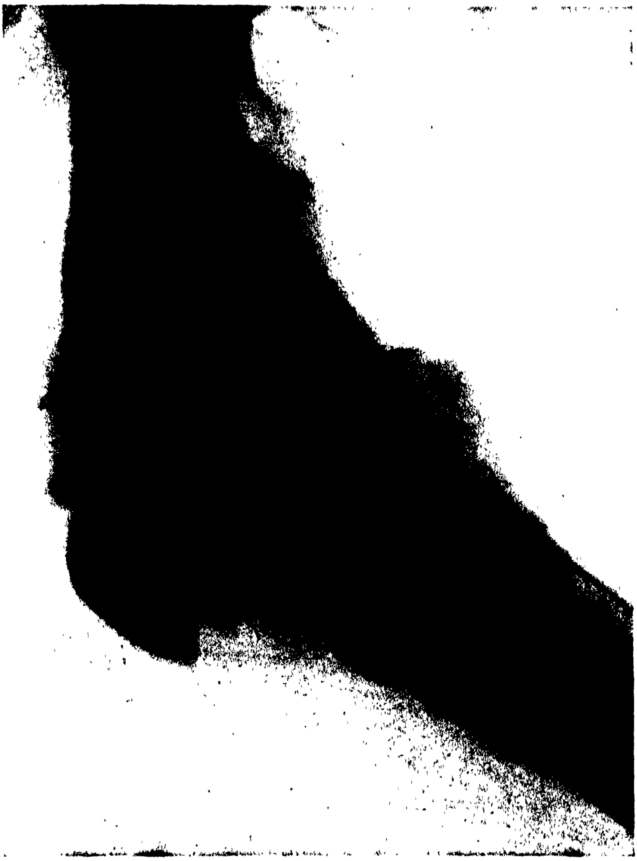


FIG. 27.—OSTEOMYELITIS OF THE FEMUR.

Differential Diagnosis.—*Syphilitic gumma* with destruction of the bone or of the joint often resembles osteomyelitis, although the pain is not as severe. In syphilis the process is more extensive than the discomfort or pain would suggest. The *x*-ray will show syphilitic characteristics. In doubtful cases the blood examination will aid in making a diagnosis.

Tuberculosis of the bone is in the epiphysis, while osteomyelitis is in the shaft. In some chronic osteomyelitis cases it is hard to differentiate between the two conditions.

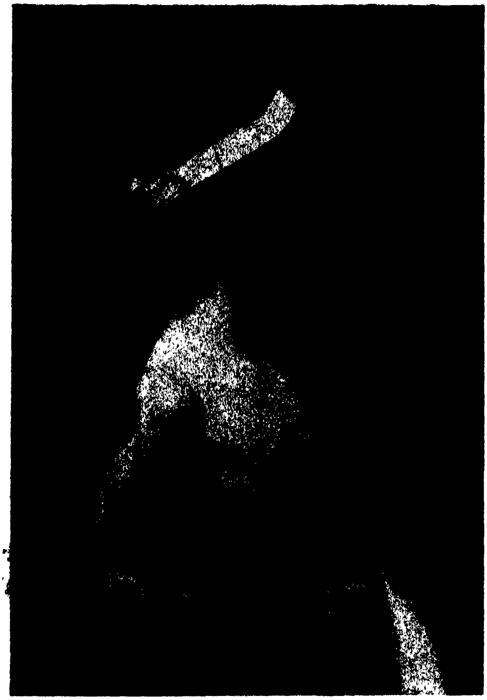


Fig. 28.—Poliomyelitis. Paralysis of the deltoid.

Treatment.—An osteomyelitis or periostitis, when not syphilitic, should be **operated** upon as soon as possible. The severe cases with delirium should be operated upon immediately, the mild cases within a few days. Judgment must be used, however, with each individual mild case and the time of operation will depend upon circumstances.

An **incision** should be made on both sides of the bone with draining down the bone and small openings into it. When it is possible, an *x*-ray examination should be made before operation, so that the exact locality of the disease may be determined.

PATHOLOGY.—The bone-marrow is primarily affected. The process may be spread extensively in the marrow before it pierces the cortex. Suppuration is produced between the bone and the periosteum. Later an abscess is produced in the soft parts. This may evacuate, draining through a sinus. It is an infection of the bony cortex. It may be limited to this cortex or involve the periosteum, or the cortex, and extend to the bony canal.

Typhoid Spine.—In this condition there is pain, disability and stiffness in the spine following typhoid fever. The temperature is slightly elevated but irregularly so.

FIG. 29.—DEFORMITY OF THE SPINE DUE TO POLIOMYELITIS. Note the extreme paralysis of the back and leg muscles.

TREATMENT.—The treatment consists in general **hygiene, rest, heat,** gentle **massage** and later a light **support** and **exercises** to strengthen the back muscles.

Infantile Paralysis.—ETIOLOGY.—Infantile paralysis is an infectious disease. It may occur at any age, but usually it appears in childhood.

SYMPTOMATOLOGY.—At the **onset** there is usually fever, pain, and tenderness at the back and extremities, vomiting and convulsions. The paralysis comes on shortly after the other symptoms and quickly reaches its maximum. It then usually remains stationary for a variable period, lasting from a few days to several weeks. Sometimes the paralysis is noted without any other symptoms (Fig. 28). If the condition is not treated, a permanent stationary period is reached, during which the deformities and contractures occur. The paralysis is usually motor and is of the flaccid type. The paralyzed limb may be cold and bluish, and atrophy begins soon after the paralysis and may be quite marked. The reflexes are lost, depending upon which nerves are involved (Fig. 29).

After a few months, when all improvement in the paralysis has ceased, the deformities begin to appear. These may be due alone to atrophy of the muscles or to position, to superincumbent weight, to the contraction of uninjured muscles, whose opposing groups have been paralyzed; or to unequal growth. The deformities occur most often in the legs and spine (Figs. 30 and 31). If paralysis is complete, a flail-like deformity of the leg results. This is not usually the case.

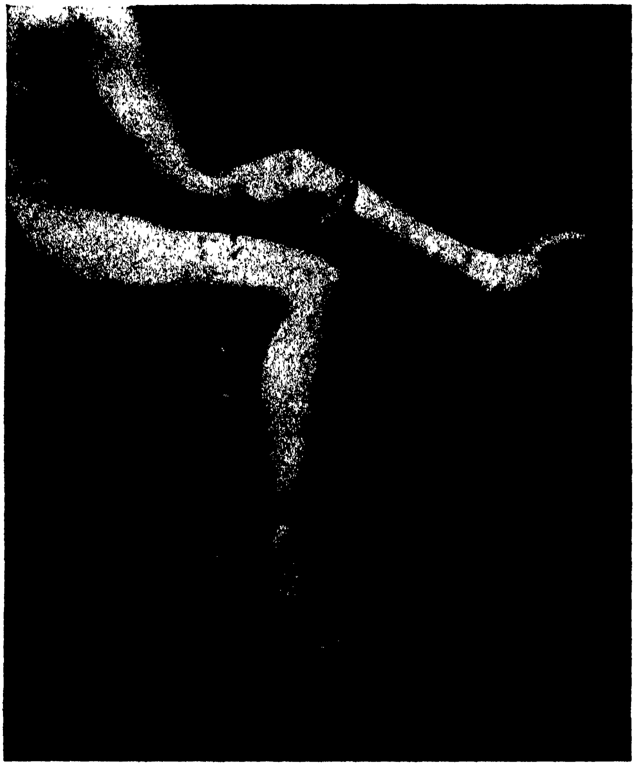


FIG. 30.—INFANTILE PARALYSIS WITH EQUINOVARUS DEFORMITY.

There may be flexion of the thigh, with knee-flexion. If all the muscles are lax there is hyperextension and lateral motion in the knee, and the weight is often borne on the ligaments. The tibia may be dislocated anteriorly or subluxated.

Talipes equinus or equinovarus, talipes calcaneus and calcaneovalgus are the common deformities of the feet. Later curvature of the spine may result from the tilting of the pelvis due to paralysis of one leg, or to faulty position due to paralysis in some other locality, or to unilateral paralysis of the muscles of the back or abdomen.

Dislocation of the hip may be present, due to either complete laxity of all of the muscles, or to unequal tension of the muscles.

The very mild cases may be extensively paralyzed at first, and then recover completely, or completely except for a few muscles.

TREATMENT.—*General Treatment.*—During the acute stage care should be directed to the general condition. The patient should be given as much **food** as he can assimilate, in small and frequent quantities, to prevent lowering the vitality. The **limbs** should be **wrapped in cotton** and the pressure of the bed-clothes prevented by **cradles.** Small quantities of **alcohol** should be given **internally.** During the paralytic stage the treatment should be directed toward the prevention of deformity and the regaining of muscle-power. The general procedure in preventing deformity is to gently **stretch** and **move the extremities** in the normal arc of joint-motion, by means of suitable apparatus. **Muscle-training, massage, baking,** etc., will help to restore muscle-power.

FIG. 31.—BRADFORD FRAME AND LONG CALIPERS APPLIED TO THE LEG.

Mechanical and Operative Treatment.—A great deal can be done by mechanical means to correct deformity, maintain correction and to aid in locomotion. Operative measures are available for the relief of contracture, for stabilizing joints, for correction of deformity and for redistribution of the unparalyzed forces by means of tendon and muscle transference.

Slight cases can be benefited to a very considerable degree. Even cases with complete leg, back and abdominal paralysis can usually be helped. In many of these extreme cases, if the hands and arms are spared, locomotion is possible by means of apparatus.

Very much can be done to improve the condition of the patient who has been crippled in consequence of poliomyelitis. So much is available that it is a question requiring only study of the case, experience and some judgment to make a choice of procedures.

PROGNOSIS.—The prognosis as to life is good in the spinal type. In the ascending type with medullary involvement, the prognosis is poor, death resulting usually from respiratory paralysis. The prognosis as to deformity is more favorable under treatment and where the paralysis is not too extensive.

PATHOLOGY.—The disease is a hemorrhagic myelitis, usually involving the cells of the anterior horn. Atrophy of the muscles follows the degeneration of the cells. The extent of the muscular atrophy depends upon the extent of the spinal injury. The process is usually limited to the spinal cord but may involve the medulla and the brain. The muscles, skin, bone and all of the tissues may atrophy, depending upon the amount of cord involvement.

NON-INFECTIOUS PARALYSES

Cerebral Spastic Paralysis.—In cerebral spastic paralysis there is a loss of brain substance from hemorrhage, thrombosis, embolism, or following an acute infectious disease such as certain cases of syphilis and cerebrospinal meningitis. The reflexes are increased, and there is a tonic contracture of the affected muscles, aggravated by intentional effort. The condition may be hemiplegic, diplegic, paraplegic or monoplegic.

The intelligence is sometimes affected, either slightly or extremely. The child may be only backward, or idiotic. Sometimes epilepsy is present from the start, or it may develop as the child grows older. Often it will disappear in adult life. If the case is not treated there is more or less paralysis of motion, and slight or extreme contractures and deformities, due to the tension of the affected muscles (Fig. 32). The disability will depend upon the rigidity, the coördination and the deformity. The most common contractures are flexion of the hip, knee-flexion, subluxations of the knees, equinus, inward rotation of the shoulder, pronation of the forearm and flexion of the wrist.

Almost all of the deformities are possible, but the above are the more common. In extreme cases patients cannot coördinate enough to use their arms or legs voluntarily—they cannot sit up or move. Fortunately these patients are usually idiotic, and so do not realize their condition.

TREATMENT.—In mild cases, they may be enabled by **muscle training** and the proper and **intermittent use of braces**, to coördinate so well that the condition cannot be noticed. Patients who cannot walk because of contractures may be relieved by **operation**, after which braces may be used which will help in locomotion. By training in coördination the braces are gradually rendered unnecessary. Almost all cases may be improved. The slight cases are greatly improved. **Tenotomies, myotomies, fasciotomies, tendon-transplantation, silk ligament** and **tendon-fixation** are all operative measures of value in special cases.

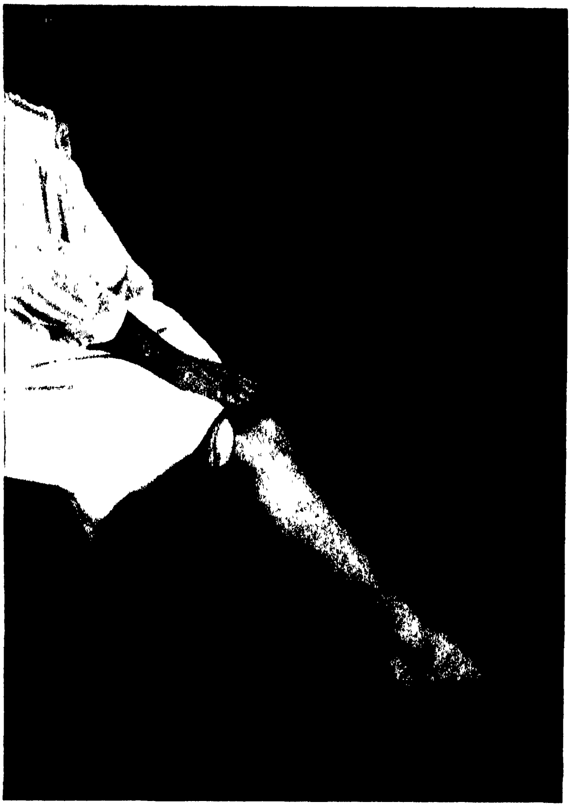


FIG. 32.—SPASTIC EQUINUS.

Spastic Spinal Paralysis.—Spastic spinal paralysis is due to a degeneration or lesion in the pyramidal tracts. The condition is similar to the spastic condition due to cerebral spastic paralysis, but there is no cerebral involvement and the prognosis is more favorable.

Obstetrical Paralysis.—Obstetrical paralysis is due to the stretching, tearing or crushing of the brachial plexus at birth. There is hemorrhage or rupture in the nerve-sheath between the clavicle and the first rib. There are three types: the upper arm type, involving the fifth and sixth cervical nerves; the lower arm type, which is very rare; and the complete arm paralysis. In the upper arm type the injury is in the nerve-plexus, or above it close to the intervertebral forearm. The shoulder-muscles and those of the upper arm are weak or paralyzed. The arm is short. The forearm escapes, although it may be weak. In this type there may be adhesions or luxations about the shoulder. If the forearm muscles are weak, they may be trained and developed. The deltoid, infraspinatus serratus, teres major and minor, biceps, brachialis anticus, supinator longus and brevis, and coracobrachialis are affected, varying with the nature and extent of the condition.

TREATMENT.—The treatment consists in **muscle training, exercise,** with **support** to prevent overstretching of the weak muscles, **manipulation, stretching of the shortened muscles,** and in cases with contractures, of **muscle lengthening** or **myotomies** as the case requires. Myotomy of the subscapularis (the Sever operation) is indicated.

In the forearm and arm types, **exercises, manipulation** and **massage** are sometimes beneficial. In the new-born the pectorals and inward rotators and adductors of the shoulder should be gently **stretched** several times a day, also the flexors of the elbow, wrist and fingers and the pronators of the forearm. This will allow the unaffected muscles a chance to grow, and will also prevent severe contractures which might render function difficult.

OTHER PATHOLOGICAL CONDITIONS OF THE BONES

Progressive Muscular Atrophy.—There are several types of progressive muscular dystrophy or atrophy which deserve separate mention.

HAND AND FOREARM TYPE (*Aran-Duchenne*).—This form occurs in adults over twenty-five years of age and very rarely in children. The anterior horn of the cord is involved. There is a little pain, and loss of power and atrophy of the hand, especially of the thenar and hypothenar muscles of the hand. The interossei lumbricales, the flexors and extensors of the forearm atrophy. In the later stages there is a condition of muscular contracture, and a characteristic claw-hand deformity. The body and lower extremities atrophy and sensation is unimpaired.

PERONEAL TYPE.—The peroneal type is hereditary, and occurs early and practically always under the age of twenty years. There is no cord lesion. It is a peripheral motor-nerve degeneration, affecting the nerves controlling the muscles of the hands and feet. As atrophy progresses there may be deformity and slight hyperesthesia. Sensation is rarely impaired.

ANGEL-WING TYPE.—Juvenile atrophy (Erb) occurs in later childhood and involves the serratus magnus, the pectoralis, trapezius, rhomboidei and latissimus dorsi. These muscles weaken and later atrophy, causing the characteristic "angel-wing" deformity. The back, thigh, and later the lower leg muscles gradually weaken. The disease process is very slow and does not progress sufficiently to give a total paralysis. The condition is incurable.

LARGE CALF TYPE.—Pseudomuscular hypertrophy occurs between the ages of five and ten. There is a marked muscular weakness in the thigh and back, with atrophy and weakness in the leg, and enlargement of the calf due to the presence of fat and fibrous tissue, giving the appearance of strength here. The arms are only slightly affected. There is a shuffling gait and great difficulty in rising from a prone position. Sensation is not affected. There is no recovery and very few live beyond young adult life.

FACE AND SHOULDER TYPE (*Landouzy-Déjerine*).—The face muscles are atrophied, giving a dull, flaccid appearance. The muscles of mastication and of the eye are never affected. The atrophy spreads to involve the shoulder and arm muscles.

These types may be divided into the (*a*) myopathic, including all but the Aran-Duchenne cases, and (*b*) myelopathic, consisting of the Aran-Duchenne cases. The latter are classed as myelopathic.

Infantile Scurvy.—This condition may be slight or severe. In mild cases there is debility, and poor physical condition. As in orthopedic conditions, the patient is usually brought for treatment suffering from pain or fracture in the long bones. With this pain, which may be extreme, there is anemia, spongy gums, purpuric spots, and swelling along the painful areas. *X*-rays show subperiosteal hemorrhages and often more or less complete fractures. The spine is rounded outward and backward, and in extreme cases the infant has thin, senile features.

TREATMENT.—The child should be kept quiet on his back on a **Bradford frame** so that he may be moved without jarring the tender extremities. A curved frame may be used. The patient should be given **small** and **frequent feedings** adapted to his age, with **orange juice** twice daily. The improvement is usually very marked in six or eight weeks.

Congenital Torticollis.—Congenital torticollis is an asymmetrical carriage of the head on the shoulders due to the asymmetrical development of the vertebræ or ribs or to asymmetrical pull or development of the muscles. There is usually a facial asymmetry due to the unilateral pull. This in time becomes less pronounced. There is rarely any pain. The movement of the head is very much or only slightly restricted to one side. When it is the muscles which are affected, the sternomastoid is more frequently found to be contracted than any other muscle. The posterior muscles may be contracted with or without the anterior.

TREATMENT.—**Stretching, massage,** and **exercises** are of little and **only very temporary value.** The treatment of choice is **section of the contracted muscle,** including its anterior and posterior sheaths. No fibers should be left uncut. This may be done through a very small incision, as the skin just above the clavicle may be stretched outwardly or inwardly and the entire sternomastoid muscle easily reached. The important element of cure is to hold the head in an overcorrected position by **apparatus** for from ten to twelve months after operation (Fig. 33). The results are uniformly successful. When the condition is due to bony malformation or to asymmetry which cannot be corrected by exercises, further asymmetrical development may be prevented and the growth guided in the right direction by a **brace**. Neglected cases of congenital torticollis produce chest and spinal deformities in time. It is therefore important to treat the cases as early as is practical. Operation is rarely advisable until the patient is about five years of age.

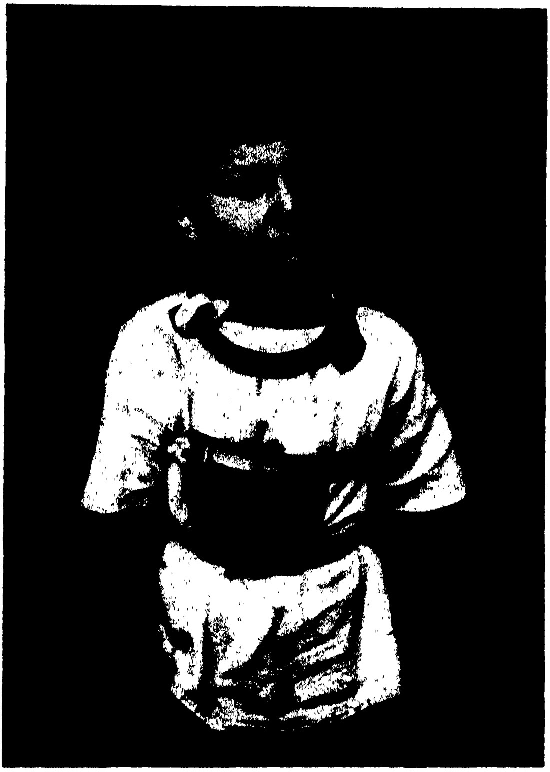


FIG. 33.—TORTICOLLIS, SHOWING POSTOPERATIVE BRACE.

Acquired Torticollis.—Acquired torticollis generally begins in childhood, except the spasmodic form which occurs in adults.

ETIOLOGY.—Acquired torticollis may be due to acute infection of the glands or of other tissues of the neck. It may be attributable to direct limitation of the muscles or to reflex irritation of the nerves, occurring in nasopharyngeal or ear diseases, or in arthritis. The spasmodic type is of unknown etiology. Torticollis sometimes results from deep scars due to bursitis or to other trauma. Unequal vision, and faulty attitude in working, may be causes. Typesetters are of this class.

TREATMENT.—The treatment is at first to combat any obvious cause. If the torticollis is well established, **rest, exercises, braces** and **jackets** will aid in the correction of the deformity.

In spasmodic torticollis the treatment is by fixation. **Resection of the spinal accessory nerve** has been recommended, also **myotomy** of most of the neck-muscles. This should be resorted to very rarely, if at all. Resection of the sternomastoid muscle is not sufficient, as in acquired torticollis too many other muscles are involved.

Sciatic Scoliosis.—There may be changes in the contour of the spine due to chronic sciatica. The patient will bend away from the painful part, adducting the affected limb to relieve the tension on the nerves. There results, if this condition is chronic, a lateral lumbar curvature with the convexity opposite the affected limb. At the same time there is a loss of the normal lumbar lordosis. Later there may be a compensating curvature higher up in the spine.

TREATMENT.—It is necessary first to **find** the **cause of the sciatic pain and to relieve it.**

If the condition is due to strain it should be treated in the same way as sacro-iliac injury and other lame back conditions. As the back improves the sciatica will improve as well. The possibility of arthritis, proliferative, toxic or infectious, must not be forgotten.

Back-strain.—Back-strain is a condition often described by various authors under the names of irritable spine, hysterical spine, weakness of the spine, etc.

ETIOLOGY.—The condition is most common in adolescent and young adult women, and is rarely found in children. It usually affects patients who are under par physically, or who are of an emotional and excitable temperament or have been subject to business strain or social high tension. Most authors describe the affection as being the result of trauma, or of overuse or overstrain of the back-muscles.

SYMPTOMATOLOGY.—Pain is prominent as a symptom. There is also irritability and sensitiveness in the spine. All symptoms are aggravated by voluntary motion. There is often muscular rigidity. This may be unilateral.

TREATMENT.—Treatment should be directed toward the cause of the affection. The back-muscles should be rested by **recumbency.** When it is necessary the patient should recline for a part or all of the time at first. Later the back may be supported by a **brace corset** or by **adhesive strapping** temporarily and by recumbency part of the time. The real means of cure consists in **exercises** which cultivate a correct standing position.

Osteogenesis Imperfecta—Fragilitas Ossium.—Infants with osteogenesis imperfecta rarely live over a year. Occasionally they live beyond childhood, but only rarely. The bones are very brittle, multiple fractures occur in a short time; often they are painless. All of the bones are equally susceptible. The callus formation is small; the medullary cavity is increased at the expense of the cortex. The bones of the skull ossify imperfectly. In the long bones, the trabeculæ show imperfect bony lamination; the corpuscles are oval, not stellate. There are no canaliculi between the lacunæ.

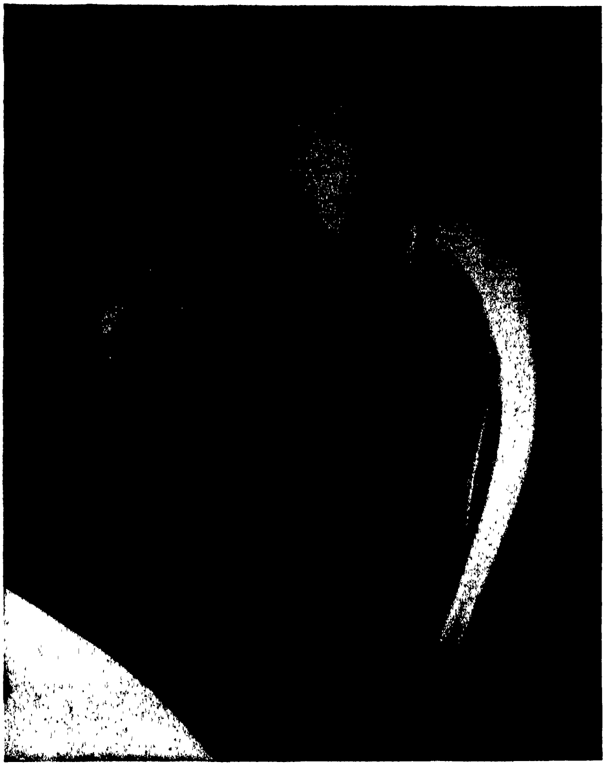


Fig. 34.—Osteomalacia, Showing Spontaneous Fracture of the Femur.

Osteomalacia.—Osteomalacia occurs chiefly in adult life, although sometimes in childhood. The bones bend and break easily (Fig. 34). The condition is one of faulty nutrition, with a decrease in lime salts and phosphorus in the bone, a richness in magnesium, and an increase in sulphur. The shaft and ends of the bones are affected alike. The bones are thinned and softened.

Treatment.—The treatment is unsatisfactory. It consists of general hygienic exercises and care in the diet.

Osteitis Deformans (Paget's Disease).—In Paget's disease the bones soften, enlarge and curve. It occurs in later life from forty years of age on. It is usually accompanied by a certain degree of arteriosclerosis. There may be intense pain in the curving long bone. The tibia is more apt to be affected; it becomes rounded and saber-shaped (Fig. 35). The patient walks stiffly and awkwardly as the condition progresses. The back becomes round, the head enlarges, and the bowing of the whole leg increases.

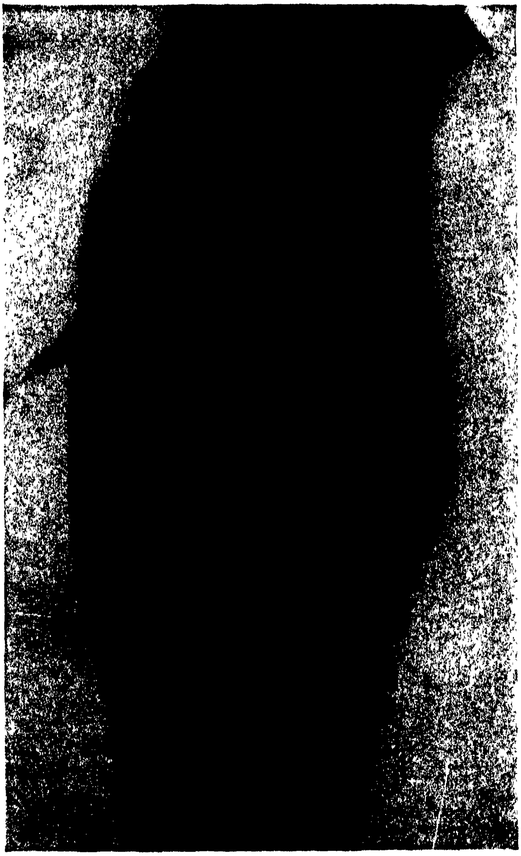


FIG. 35.—PAGET'S DISEASE.

TREATMENT.—General **hygiene** and **local heat** and **flannel** protection help to decrease the pain.

Painful Heel—Bursitis (Policeman's Heel).—There is pain and sensitiveness at the bottom of the heel. This may be due to undue pressure at that point, or to an inflammation of the bursa under the os calcis, or to sudden or prolonged strain at the attachment of the plantar fascia. This condition should not be confused with disease of the bone or periosteum. An x-ray examination will aid in diagnosis.

TREATMENT.—The treatment consists in **removing the pressure** or in modifying it by pads; in extreme cases, **immobilization**, and, when the patient is walking, **poultices** and **counterirritants** will be necessary.

Ingrown Toe-nail.—TREATMENT.—**Operation** under local or full anesthesia is indicated. A **tourniquet** may be applied at the base of the toe. The overlapping tissue is removed by two parallel longitudinal incisions. One incision splits the nail a full quarter of an inch from its lateral edge and is continued through the matrix to the bone. The other, running parallel to the first, is made through the skin beyond the nail, and is carried down to the bone. These parallel incisions are continued through the base of the nail for nearly half an inch, but should not reach the joint. The nail and tissue between these incisions are removed (Fig. 36). The gap is closed by sutures passed through the remaining nail and the edge of the skin.

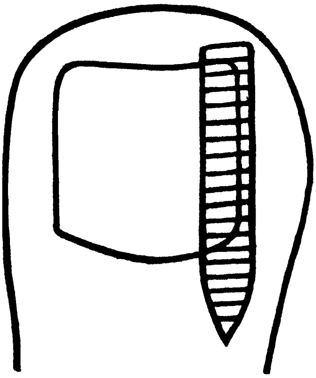


FIG. 36.—TISSUE AND PART OF NAIL REMOVED FOR INGROWN TOE-NAIL.

Hallux Rigidus.—This condition is characterized by pain and limitation of motion in the great toe. It may be due to the constant pressure of an ill-fitting shoe, to trauma, contracted capsule or to old arthritis.

TREATMENT.—The treatment includes the wearing of properly fitting **shoes**, of **local heat** and **applications**, with **protection** from all **pressure** and **motion** until the symptoms have disappeared.

Hallux Valgus (*Abduction of the Great Toe*).—TREATMENT.—When slight, this may be corrected by **exercises**, by **stretching** the ligaments, by wearing **straight-lined** shoes. When the condition is extreme, an **operation** may be necessary. The head of the metatarsal, so necessary in weight-bearing, should not be removed. **Osteotomy** may be performed, or a **wedge removed** at the neck of the bone. These operations are often contra-indicated in rheumatic patients (Fig. 37).

Hemophilic Joint Swelling.—This condition usually occurs in so-called "bleeders." The hemorrhages often occur with very slight trauma. The hemorrhage is in the tissues about the joint as well as in the joint itself.

FIG. 37.—HALLUX VALGUS.

TREATMENT.—**Rest** and sometimes **fixation of the joint** are indicated immediately after trauma and during the acute swelling. If the swelling is very slight this will not be necessary. The use of **horse serum** injected subcutaneously, not near the joint, and the judicious use of **exercises** to tone up the general condition, are indicated.

DISEASES OF THE JOINTS

Dislocations

Congenital Dislocation of the Hip.—Etiology.—In congenital dislocation of the hip, the hip may be very slightly dislocated, in which case the head of the femur slides insecurely in the acetabulum and just over its rim; or it may be markedly dislocated, the trochanter being near the crest of the ilium.

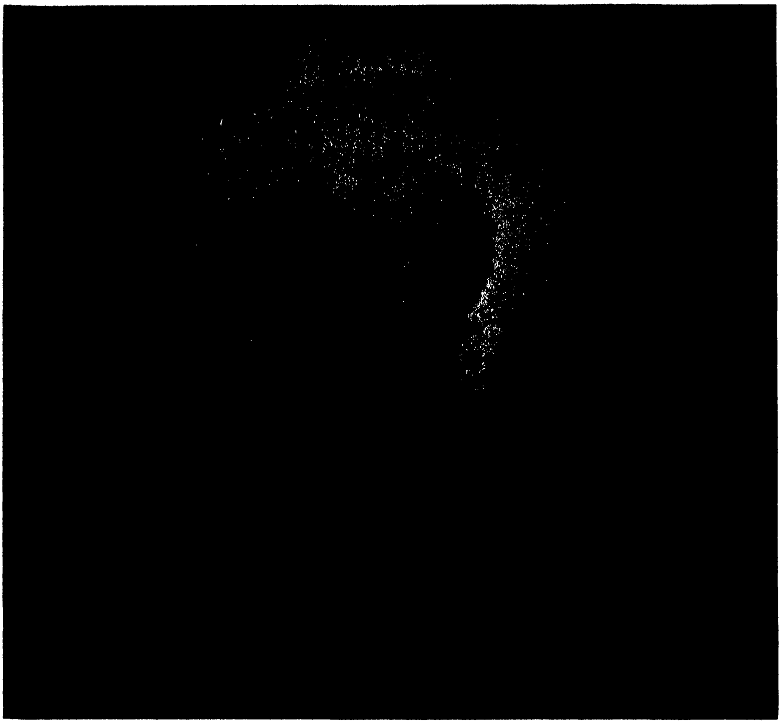


Fig. 38.—Congenital Dislocation of the Hip.

Symptomatology.—There may be little or a great deal of disability at first. Usually when the child begins to walk there is a noticeable limp which gradually increases. Later there may be a very marked rolling gait. The limp is more noticeable when the condition is single than when a double dislocation exists. The trochanter will be found above Nelaton's line (a line connecting the anterior superior spine of the ilium and the tuberosity of the ischium). The mobility of the trochanter up or down as the patient walks or as the leg is pulled, or when the patient is lying down, will be noticed. The perineum is broader. There will also be a Trendelenburg sign. (This sign is obtained by making the patient stand on one leg and raise the opposite knee. The physician faces the back of the patient and watches the line of the buttock. If the hip of the leg on which the patient stands is dislocated, the opposite buttock drops.) There is a very marked shortening of the affected leg (Fig. 38). With a dislocated hip, there is more motion. Motion in inward rotation and adduction may be extreme. The length of the capsule allows very great freedom of motion in the young child. As the patient grows older the capsule becomes shorter and there is more limitation and sometimes very little motion. The capsule is thickened and often constricted, due to the pull and due to the lack of lateral stretching of its fibers. The cotyloid ring is narrowed, making reduction more or less difficult. There is disability from the limp

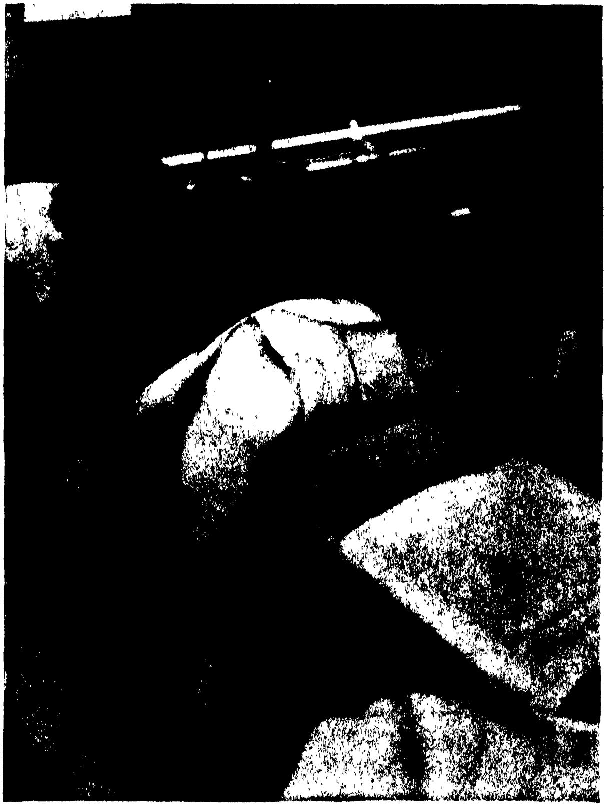


FIG. 39.—CONGENITAL DISLOCATION OF THE HIP, SHOWING POSTOPERATIVE PLASTER AND POSITION IN BED ON A BRADFORD FRAME.

and especially from the acquired deformities due to the shortening of the muscles and the later limitation of motion. Lordosis becomes extreme. There is pain in the back and often pain in the hip due to the lordosis, to the hip flexion and limitation of motion. The patient walks on the toe of the shortened leg.

An *x*-ray examination of a congenital dislocation of the hip will often show a shallow acetabulum when the acetabulum is really not shallow. This is due to the increased radiability of the cartilaginous edge. The head of the femur is often smaller, and there is more torsion in the neck than in normal cases.

DIFFERENTIAL DIAGNOSIS.—Congenital dislocation of the hip is not easily confused with other conditions, except perhaps dislocation due to acute arthritis of infancy. In this type of case the head of the bone is likely to be partly or totally destroyed and there is apt to be a small scar on the skin from one-quarter to one-half an inch in diameter where the abscess discharged itself in infancy. An *x*-ray examination will, of course, be an aid in diagnosis.

TREATMENT.—The treatment of a congenital dislocation of the hip consists in reducing the dislocation by **manipulation** under ether and in **maintaining the reduction** long enough to allow the ligaments to actually shorten and the bones to grow, so that the capsule and ligaments will tighten. The corrected position should be maintained by appliances for from ten to twelve months (Fig. 39). The best position for after-treatment is one with the leg abducted 90 degrees and flexed 90 degrees. In a case which has been well reduced, the head must be in the acetabulum and the line of the femur should be such that the knee is posterior to and above a line drawn through the anterior superior iliac spines. The best age for operative reduction is between two and one-half and seven years. By means of Dr. Bradford's congenital **hip machine**, used at the Children's Hospital in Boston and in many other cities in this country and abroad, it is possible to reduce dislocation in cases of individuals over fifteen years of age. One case was reduced at the age of twenty-four. It is inadvisable to wait longer than seven years. The patient grows older and the muscles grow strong, making the reduction proportionately more difficult.

Should the reduction by the Bradford machine fail, it is necessary, in a few cases, to make an **incision.** Operation by incision alone will not allow the head to be reduced in a congenital dislocation of the hip, unless there is some forcible means of reduction at hand to help the surgeon with the open operation. Dr. Bradford's apparatus for this purpose is most useful. Many cases may be reduced manually without a traction machine and without a congenital hip machine such as Dr. Bradford's. It is better to operate between the ages of four and eight. Cases of individuals fifteen years of age can be reduced by Dr. Bradford's apparatus. The author reduced one congenital hip at twenty-four years of age.

Whether or not the machine is used, it is important to **stretch the capsule** thoroughly before and after reducing the hip. Redislocations are often due to lack of proper capsular stretching. **As a rule, extreme cases of torsion of the neck do not need an osteotomy.** After the hip is reduced the torsion disappears in time with weight bearing. After operation, the patient is put in **plaster** which covers the pelvis, the thigh, the leg and the foot of the affected side and includes a small cuff of plaster around the unaffected thigh. It is important that the plaster should fit well and snugly cover the trochanter and the tuberosity of the ischium on the affected side, so that the plaster cannot slide up and dislocate the hip.

Snapping Knee.—This is a partial recurrent displacement of the tibia on sudden extension of the leg. The tibia is displaced forward, with outward rotation. There is often an audible snapping sound. The condition is due to weakness and laxity of the ligaments and muscles. Occasionally the sensation is produced by a slipping tendon or muscle without joint luxation. Anteroposterior relaxation following an injury is sometimes due to a torn crucial ligament.

Congenital Dislocation of the Knee.—Congenital dislocation of the knee is probably due to the position *in utero.* The ligaments of the knee are loose and the tibia is dislocated anteriorly and often laterally at the same time. When the articulation is very loose, it may be dislocated backward.

TREATMENT.—The bones should be replaced gently several times a day; with a little practice this can be done easily. If this treatment is long continued, in some cases the bones will remain in place of themselves, while in others they will have to be put in place daily in this way until the child is a year old or older. The knee is then **reduced** and held flexed by a **plaster of Paris bandage** for from six to ten months, the bandage being renewed as often as is necessary. The child is allowed to move about with the plaster on.

Congenital Hyperextension of the Knee.—Congenital hyperextension of the knee may occur with other congenital deformities such as congenital club foot, and congenital dislocation of the hip (Fig. 40). The knee is bowed backward and cannot be flexed; in some cases it cannot be straightened.

TREATMENT.—**Gradually stretching the knee** in flexion will in time overcome the mild cases. In other cases an ether **manipulation** is necessary and the knee is put in **plaster of Paris** in a flexed position, for from four to eight months. After that it is flexed regularly each day. The use of plaster of Paris should be avoided until the child is over a year old.

Congenital Dislocation of the Patella.—Congenital dislocation of the patella is often due to a lack of growth of the external condyle of the femur or to a lateral subluxation of the knee with dislocation, usually accompanied by more or less knock-knee.

TREATMENT.—When discovered early, these cases yield to the **manipulation** described under Congenital Dislocation of the Knee. If, however, the affection is not discovered until the child is six or seven years old, it is very often necessary to correct the knock-knee by **osteotomy** and to reef the patellar ligament as described under Traumatic Dislocation of the Patella.

Traumatic Dislocation of the Patella.—A traumatic dislocation of the patella is usually outward. The patella may remain dislocated for a short time, but as a rule it slips back as the knee straightens.

TREATMENT.—Occasionally the dislocation cannot be reduced without **ether relaxation**, but after this treatment the patella readily slips into place. After a traumatic dislocation of the patella, the knee should be kept entirely straight for at least five weeks in a **plaster of Paris splint.** This will prevent flexion and allow the torn ligaments to shorten up and heal. In recurrent dislocation of the patella, it is necessary, as a rule, to **split** the **patellar tendon**, cut away the lower attachment of the outer half, quilt it with silk and attach it to the inner side of the tibia. This attachment, and reefing the capsule on the inner side, will prevent future dislocation, provided the after-treatment is carefully guided for five or six weeks, to prevent much flexion of the knee.

FIG. 40.—CONGENITAL HYPEREXTENSION OF THE KNEE, AND CONGENITAL CONTRACTURE OF THE HIP.

Sacro-iliac Injury.—The sacro-iliac articulation may be injured by falls on the buttocks or pelvis, or by strains.

Symptomatology.—The symptoms are pain, limping and weakness. The pain is referred to the side of the pelvis and may radiate along the buttock and thigh. There is pain on forward bending of the body, on flexion of the thigh, or on any sudden motion or jar. There may be tenderness over the articulation.

Treatment.—Treatment is by **support**, either with **fixed plaster bandages, adhesive straps**, or by **rest in bed**. After this, mild **exercises** and **proper posture** are indicated.

Bad strains will often require from six to eight weeks to overcome the severe symptoms. Following this the back must be straightened and the general health improved. The possibility of infectious, toxic, or proliferative arthritis must not be forgotten.

Subluxation of the Clavicle.—The sternal end of the clavicle may be partially displaced. This is usually due to injury. The capsule is lax, allowing displacement during certain motions of the arm. The reduction is easy. There may be pain and discomfort as well as weakness and insecurity.

Treatment.—When not severe, the displacement may be cured by **appliances** holding the clavicle in place. The joint may be opened and a small **inlay graft** taken from the clavicle and placed bridging the sternoclavicular joint.

Congenital Dislocation of the Shoulder.—This condition is rare. Dislocation may also be due to trauma at birth. The head of the bone is usually displaced backward over the scapula with abduction and inward rotation of the arm. Dislocation following obstetrical paralysis may simulate the congenital form.

Treatment.—Treatment is by **reduction** and **fixation in plaster**, with the arm abducted and outwardly rotated.

Chronic Recurrent Dislocation of the Shoulder.—Chronic dislocation of the shoulder may be due to stretching, and weakness of the capsule, to weakness and atrophy of the muscles, to paralysis or ruptured muscles and tendons. Recurrent cases are due to an unhealed slit in the capsule. The intervals may be short or long, and there is usually no inflammatory reaction.

Treatment.—Treatment consists in **reduction, stretching** of the capsule to prevent dislocation, and **fixation** for six weeks; later **exercises** directed toward strengthening the muscles about the joint are indicated.

Recurrent Dislocation of the Patella.—Recurrent dislocation of the patella occurs when there is a laxity of the ligaments and accidental displacement of the patella outward and toward the external condyle. It is more frequent in females than in males. There is sudden, sharp pain and disability. Later there may be an effusion in the joint.

Treatment.—Reduction is by **extension of the leg and pressure on the patella**, which is gently pushed into place. The knee should then be **fixed** either by **adhesive-strapping**, or in severe cases, **in plaster** for about five weeks. **Exercises** should be given to improve the muscular tone. Succeeding displacements are apt to be attended by less pain than the original one.

The **operative** treatment is by **splitting the patella tendon** and stitching the outer half to the periosteum of the tibia, slipping the tendon first under the inner half. Operation is advisable when there are persistent recurrent attacks.

Dislocation of the Elbow.—TREATMENT.—**Reduction** should be performed early in the condition. After six weeks the adhesions are firm and reduction may be impossible. **Operation** and **arthroplasty** or **excision** are indicated when a perfect reduction is not possible or when the dislocation has existed for any length of time.

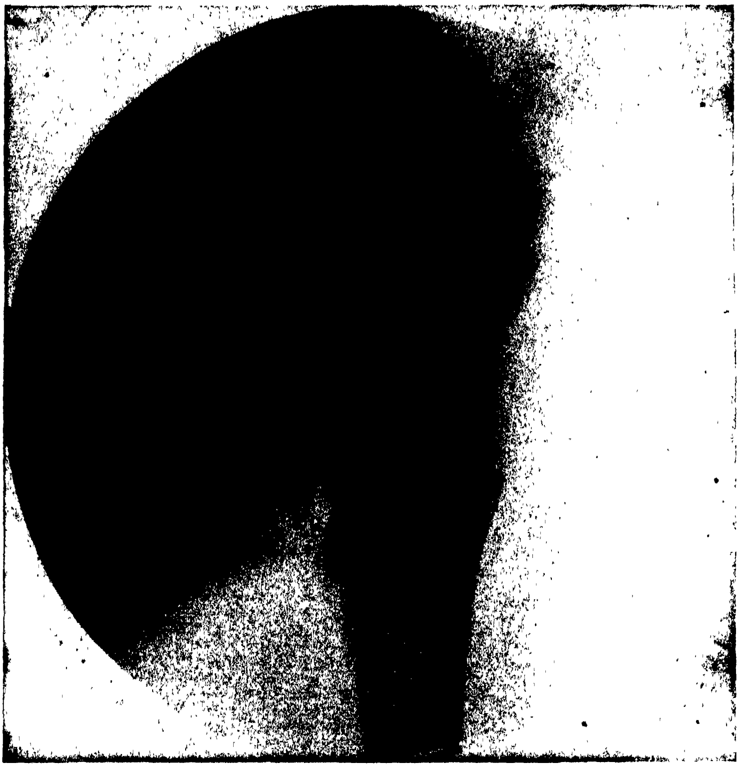


FIG. 41.—ANKYLOSIS DUE TO TUBERCULOSIS OF THE HIP.

TUBERCULOSIS OF THE JOINTS

Tuberculosis of the Hip.—ETIOLOGY.—The etiology of tuberculosis of the hip is the same as that for tuberculosis of the other bones and joints.

Symptomatology.—This disease is more common in children than in adults. The focus is usually near the epiphyseal line in the neck or head of the femur. In rare cases it may be in the trochanter and sometimes in the acetabulum. The disease is sometimes so slight that there is complete recovery with perfect motion in every direction. The disease begins with a slight limp. The child may begin early to walk on the toe of the affected leg. The pain is often referred to the knee. On examination, even early in the disease, measurements will show atrophy at the thigh, at the calf, and often at the knee. Early in the disease the x-ray will show no bony change. As the disease progresses there is apt to be muscular spasm, noticed gradually in the upper thigh muscles on the inner side of the leg, thickening in front of or behind the trochanter, or both, distinct limitation of inward rotation, and, as the disease progresses, limitation of abduction, flexion and hyperextension of the hip. There may be marked distortion and deformity of the hip. Occasionally, the patient may irritate the condition by a twist or jar, and there is extreme pain, but during the whole course of the disease pain is comparatively absent, unless an abscess is forming. Abscess may

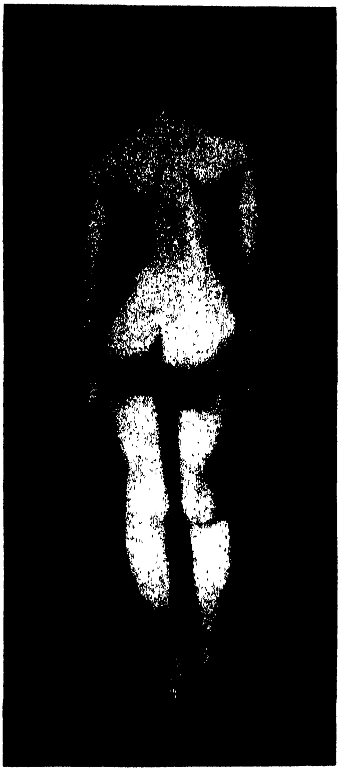


Fig. 42.—Tuberculosis of the Hip.

occur as in other joints. It may rupture spontaneously, or it may be absorbed. The abscess may burrow along the muscles and come to the surface at a joint distant from the actual site of the disease. One of the marked points of diagnosis that differentiates tuberculosis of the joint from other joint diseases is the early atrophy, which is out of proportion to the history of the disease (Fig. 41). When the disease has progressed over a long period of time there is atrophy from disuse in addition to the atrophy due to the disease. During the progress of the disease there may be so much thickening about the joint that there is no motion at the hip (Figs. 42 and 43). Double hip disease may occur. In a case that has been properly treated and is under treatment this does not signify permanent ankylosis. As the disease progresses to recovery the thickening disappears and the motion may entirely return in favorable cases.

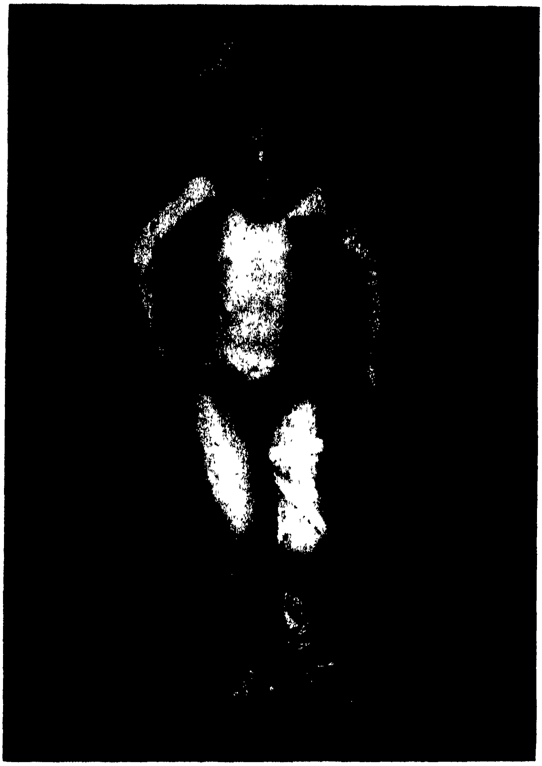


FIG. 43.—TUBERCULOSIS OF THE HIP. Acute condition.

TREATMENT.—The leg should be **fixed by traction** and by **immobilization in bed**, with the femur pointing in the direction in which it is held by the spasm of the muscles. As the spasm of the muscles decreases the leg may be brought down to the straight position. As the acute symptoms subside a well-fitting Bradford **abduction hip splint** should be applied. The patient is accustomed to these splints during the day, and the bed traction splint is applied at night. Later a high sole is applied to the shoe on the good leg and the patient is allowed to walk with a **traction splint** and **crutches**. This treatment should be kept up until there is restoration of motion and complete recovery from the disease. This may take from one to five years.

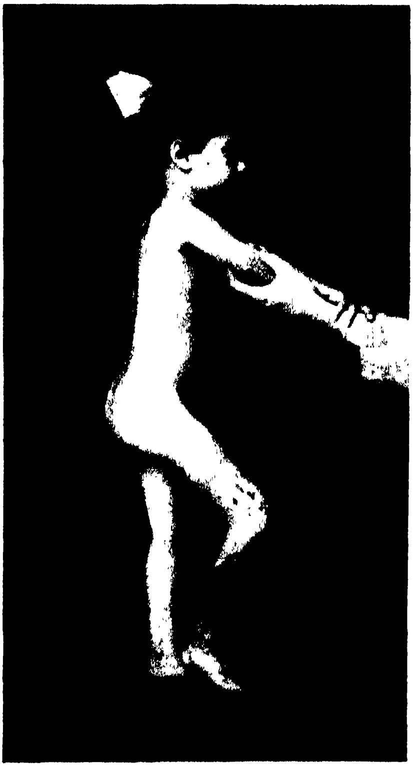


Fig. 44.—Tuberculosis of the Knee. Acute condition.

Prognosis.—Death may occur from generalized tuberculosis or from some intercurrent disease. Both are favored by poor surroundings and by the poor general condition of the patient.

The majority of cases do well under proper surroundings and hygiene, and recover with more or less deformity. The earlier the treatment is begun, and the more attention is given to the general condition of the patient, the less is the resulting deformity, other things being equal. Complete recovery without loss of motion or deformity occasionally occurs, but is not common.

PATHOLOGY.—See the Pathology of Tuberculosis of the Bones and Joints.

Tuberculosis of the Knee and Ankle.—ETIOLOGY.—The etiology of tuberculosis of the knee and ankle is the same as the etiology of tuberculosis of the other bones and joints.

SYMPTOMATOLOGY.—There is usually swelling about the joint (Fig. 44). Pain is found to be comparatively absent when the whole course of the disease is considered. Occasionally, there is slight local heat but very often there is none and the disease is characterized as a white swelling. The atrophy of the calf and thigh is very marked early in the course. When the disease is sufficiently advanced, any *x*-ray examination will show the focus and atrophy of the bone (Fig. 45).

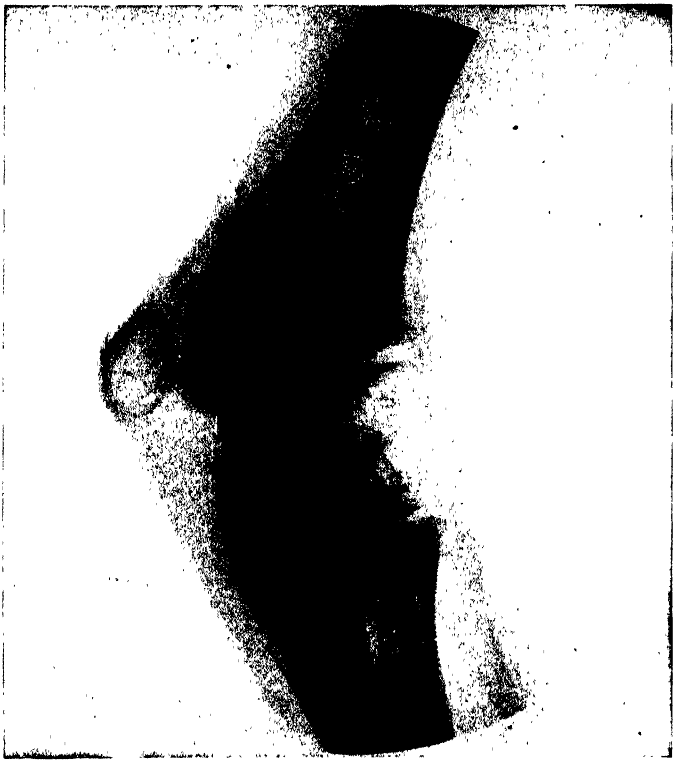


FIG. 45.—ANKYLOSIS CAUSED BY TUBERCULOSIS OF THE KNEE.

TREATMENT.—The joint should be protected from motion and jar by a well-fitting **plaster of Paris** covering and a Thomas **knee-splint.** Traction is not necessary. At night the Thomas knee-splint is removed, but the plaster is left in place. If the joints are well protected from jar and motion the disease which is at the epiphyseal line will rarely extend into the joint, even if an abscess is present. **Excision** is sometimes justifiable in adults, when the disease is extensive. In children this method should almost never be employed.

PROGNOSIS.—In children treated early in the disease there is usually complete recovery of motion. In adults, the progress of the disease is slower and there may be joint involvement early in the course.

PATHOLOGY.—The pathology of tuberculosis of the knee and ankle is the same as that discussed under the Pathology of Tuberculosis of the Bones.

Synovial Tuberculosis.—Synovial tuberculosis occurs primarily, or secondary to tuberculosis of the bone. If the joint is opened, a hypertrophied, diseased capsule with more or less fluid will be found.

TREATMENT.—**Incision** and removal of the focus, if local, is often indicated. When this is not effective, it may be necessary in extreme cases to **remove** the whole **capsule** and synovial membrane and to attempt to obtain ankylosis by erosion of the joint.

Rice Bodies.—Rice bodies are small, white, lentil-shaped or ovoid bodies sometimes found in disease of the synovial membrane of the joints, or in tenosynovitis. They are more apt to be present when the disease is tuberculous.

There is usually a peculiar crepitus about the tendon sheath in this condition, but when the bodies are present in the joint they are usually found during an operation on the joint.

SYMPTOMATOLOGY.—The symptoms are usually weakness, and inability to use the affected joint or tendons with any great force or precision. The patient complains of disability and discomfort, and later the swelling is noticed.

TREATMENT.—The tendon sheath or synovial cavity of the joint should be **incised**, the **rice bodies pressed out** and the cavity **washed out**. In extreme cases the synovial membrane or **sheath** must be completely **removed.**

Tuberculosis of the Shoulder.—For tuberculosis of the shoulder, elbow and wrist, see Treatment under Deformities of these joints.

ETIOLOGY.—See under the other joint diseases.

SYMPTOMATOLOGY.—Pain, tenderness, atrophy and limitation of motion are noted. The onset is insidious and the disease is chronic. There may be an abscess as in disease of the other joints.

TREATMENT.—In tuberculosis of the shoulder, the best position for **fixation** during the treatment is with the arm abducted 45 degrees. The general treatment is the same as that for any tuberculous joint.

PATHOLOGY.—See under disease of the other joints.

Tuberculosis of the Elbow, Wrist and Ankle.—ETIOLOGY.—See under disease of the other joints.

SYMPTOMATOLOGY.—There may be pain and tenderness. There is limitation of motion, chiefly of extension and later of flexion, supination and pronation. There is swelling of the joint, with atrophy of the muscles. A tuberculous abscess may complicate the condition, as in disease of the other joints.

TREATMENT.—In tuberculosis of the elbow the best position for **fixation** is with the elbow at right angles and the forearm very slightly pronated.

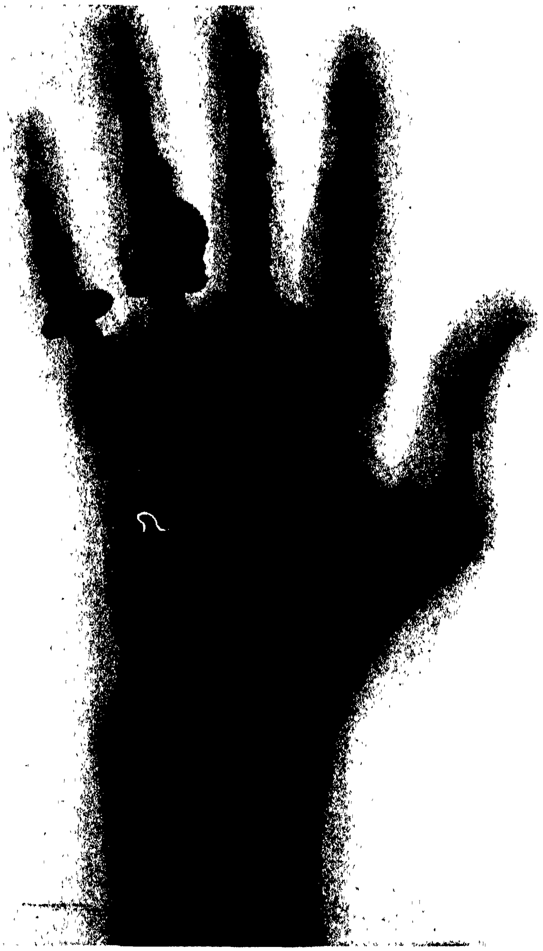


FIG. 46.—ARTHRITIS DEFORMANS.

In tuberculosis of the small bones of the wrist and foot, if the disease does not subside markedly after prolonged fixation, an **excision** of the focus is usually followed by relief. In disease of the wrist, when an excision is necessary a complete excision of all of the bones of the wrist gives a much better result than excising one diseased bone only.

PATHOLOGY.—See under other joint diseases.

ARTHRITIS OF THE JOINTS

Arthritis—Osteo-arthritis—Arthritis Deformans.—The terminology used in dealing with the various forms of arthritis has never been definite enough to be helpful, unless it is supplemented by a description of the disease. The physician will find that the nomenclature is used differently by almost every writer. It is important to distinguish clinically between certain forms of arthritis, and it is with this in view that the author will describe the following conditions, using the nomenclature approved by Dr. E. H. Bradford, Professor of Orthopedic Surgery at Harvard University Medical School. Dr. Goldthwait's clinical classifications, whatever their faults, are the most satisfactory for distinguishing the types present in various individuals. Dr. Edward H. Nichol's pathological research on the arthritic joints has helped the author to classify and treat the cases with increasing satisfaction. The cases

FIG. 47.—ARTHRITIS DEFORMANS, SHOWING INVOLVEMENT OF THE KNEE.

observed in large clinics will often include more than one type, occurring in the same individual (Figs. 46 and 47). It is possible for all types to be present in one case, but each form will be found to have a separate history, and will act in the main according to the type to which it belongs. The following classification will be found to be fairly simple and useful for the clinician, although no classification offered so far has been altogether satisfactory.

Degenerative or Atrophic Arthritis.—ETIOLOGY.—This condition is polyarthritic, affecting first the small joints, fingers, wrist, elbows, knees, tarsus, shoulder, jaw and spine; the hips are rarely involved. This form of arthritis occurs in young adult women more frequently than in men, only the highly civilized—those living a high-strung nervous life—being usually affected.

Grief, nervous shock, physical and mental strain, are important factors. The daily strain upon teachers of caring for forty or fifty children in one room, while teaching at the same time, poverty, responsibility, the physical strain of household duties, a nervous temperament with poor physical strength, all predispose to the disease.

SYMPTOMATOLOGY.—Pain is not severe, there is no "soreness" as in the infectious type of arthritis. At first there is a boggy swelling about the joint, later atrophy; this is noticed characteristically in the hands, where the atrophy between the metacarpals is characteristic. There is fixation, due later to erosion, but in the earlier stages due to habit of position and to degenerative changes eliminating the elasticity and range of motion of the joint. There may be subluxation at the knee, and joint motion may be jerky, due to erosion, and to lack of elasticity in the tissues. There is no local redness, although there may be local tenderness, slight local temperature, and slow progressive disability and deformity. Any constitutional disturbance is due to inactivity. Malnutrition and poor circulation are early noticed, also dry skin, dry nails, general debility, constant joint discomfort, low pulse and absence of fever; the hemoglobin is usually high until the debility is marked; there is very little change in the blood.

TREATMENT.—The treatment consists in attention to the **general nutrition,** to **increase in the food,** and to the **local circulation.** Indigestion may make it necessary to feed the patient often with small amounts of nourishing food. The deformities are gradually straightened by **splints** and **plasters.** One should **avoid antirheumatic remedies,** as well as **salicylates** and **iodids. Aspirin** helps some cases, also **massage** between the joints, **heat** and Bier's **hyperemia treatment.** A **warm climate** in winter is often advisable.

PATHOLOGY.—All of the joint structures are involved—cartilage, bone synovia, and the synovial fluid. The synovial membrane is affected early and thickens. The villi tips are swollen, and there is a red-cell infiltration and a reddish-purple appearance due to passive congestion. Following this, fibrous tissue formation replaces the passive congestion. Vascularity becomes less and less, and degenerative changes are marked.

The cartilage is dull in color, and there are small, erosive, degenerative areas with no inflammation about the erosion. Bony changes come late. The intratrabecular fat is increased, and the trabeculæ are diminished in number; later rarefaction of the bone and obliteration of the cartilage take place; there is no increase in the joint fluid. Bone and cartilage deposits appear in the villi of the synovia.

Proliferative or Hypertrophic Osteo-arthritis.—ETIOLOGY.—Trauma and exposure to extremes of temperature or humidity are prominent predisposing factors. The disease is found in firemen, teamsters, refrigerator plant workers, longshoremen, heavy load workers, and in conjunction with arteriosclerosis, in elderly people. Spine lesions are more common in this latter variety. Involvement of the elbow is found in baseball players.

SYMPTOMATOLOGY.—There is no constitutional disturbance. When the condition is first discovered there are no marked changes visible on the x-ray plate. Pain is usually the result of slight or severe trauma or of motion out of proportion to the range of the joint; as the pain disappears a bony enlargement is noted, also deformity and lameness. Digestive disturbance, flatulence, and constipation are frequent.

The hip and knee cause more disability than do the other parts. The lipping is observed at the edges of the joints of the knee, spine, feet, patella, and hip (morbus coxæ seniles). There is limited motion, due to the proliferation of bone about the joint; later deformities occur in all the affected joints.

TREATMENT.—Treatment consists in **local heat** and in **correcting mechanical faults** in the use of the joints, to prevent deformity. Attention must be paid to **digestion** and to the condition of **bowels and kidney. Protection** and **rest** during the acute symptoms, Bier's **hyperemia treatment,** careful **massage** above and below the joint, avoiding the joint, **sodium phosphate** and **olive oil internally** are important. **Plaster of Paris bandages** are indicated when there is much pain.

PATHOLOGY.—In the young there is thickening and infiltration about the joint ligaments, with very few joint and cartilage manifestations. In middle life the cartilage and osseous tissue are affected; there is little synovial change; the cartilage proliferates. Thickening occurs on the dorsum of the terminal phalangeal joints; when the disease is pronounced there is a marked lipping and osseous spurs about the joint, noticed especially at the knee, the spine and the hip. The bone is normal at first; later there is a mechanical erosion due to the spurs. There are no inflammatory deposits in and about the erosions.

The lesions are slow and require years for their formation.

Infectious Arthritis (Nontuberculous).—ETIOLOGY.—This type of arthritis is due to bacteria or their toxic products. It is a systemic toxemia with joint infection. There may be almost no constitutional symptoms. Disease of the ear, throat, teeth, eyes, heart, glands, abdominal organs, intestine, pelvic organs, prostate, seminal vesicles, respiratory system, and epidemic infections, may cause the condition. Usually, but not always, the onset is sudden. The joint involvement may follow in a few days or somewhat later. The condition is usually polyarticular; the original joint may clear up early in the disease.

Symptomatology.—There is swelling, pain, limitation of motion, loss of function, and spasm followed by deformity. Often there is general glandular and splenic enlargement. Secondary anemia, slight temperature, high pulse, loss of flesh and loss of sleep are noted.

Treatment.—All sources of **infection** should be sought for and **eliminated**. The **local resistance** should be increased. The inflammation may be reduced by **heat**, local applications, and **fixation** to eliminate spasm. Suppurative cases will require **operation**. All abscesses should be freely drained. **Manipulation** to relieve stiffness will give good results only when the adhesions are not too extensive. Deformity in flexion with joint motion is often best treated by **osteotomy** (see Treatment of Deformities). **Braces** are often very helpful in correcting deformity and in fixing the joint while it is sensitive. As the acute symptoms subside the circulation and muscle tone should be improved by **massage**, omitting the joints, and by the judicious use of **exercises**.

Pain is best relieved by **heat**, **fixation** and **rest**, and in suppurative cases by **drainage**. Bodily strength should be increased by hygienic measures and **diet**, and by **tonics** after the acute stage is over.

Antitoxins and **vaccines** are usually of **doubtful value**; in some instances they have helped greatly. It should be remembered that an osteomyelitis in the vicinity of a joint may be mistaken for an infectious arthritis.

Acute Arthritis in Infancy.—Acute arthritis in infancy is an acute infectious process in the hip epiphysis; the process is destructive and the hip usually dislocates. A small abscess discharges in the vicinity of the trochanter, usually posterior to it. An examination will show a dislocation with complete destruction or separation of the head or, in some cases, a dislocation only. The condition is usually secondary to some infectious disease such as scarlet fever, inflammation of the middle ear, or pneumonia. Very often the local process is not noticed until the child recovers from the original infection; the hip is then found to be dislocated. It is an infection of infancy.

When the head of the joint is not destroyed or only partially so, the hip may be treated in the same way as for a congenital dislocation. The acute symptoms are acute pain, swelling, tenderness, local heat, spasm, and high temperature. The constitutional symptoms are often attributed to the original disease and the local condition not noticed. As soon as the condition is recognized it should be **operated upon**. Dislocation of the hip has often been prevented in this way.

Gonorrheal Arthritis.—Gonorrheal arthritis is an inflammation of the joint following gonorrheal infection. In many cases the original gonorrheal infection has disappeared and the joint condition has followed a remote or obscure latent focus, for instance, in the pelvis or seminal vesicles.

The condition may affect one or many joints.

Symptomatology.—There is usually pain, swelling, local heat, disability, spasm, limited motion, and swelling of the capsule. In subacute cases there is discomfort, weakness, swelling and disability. When the seminal vesicles are involved there may be no external evidence of disease.

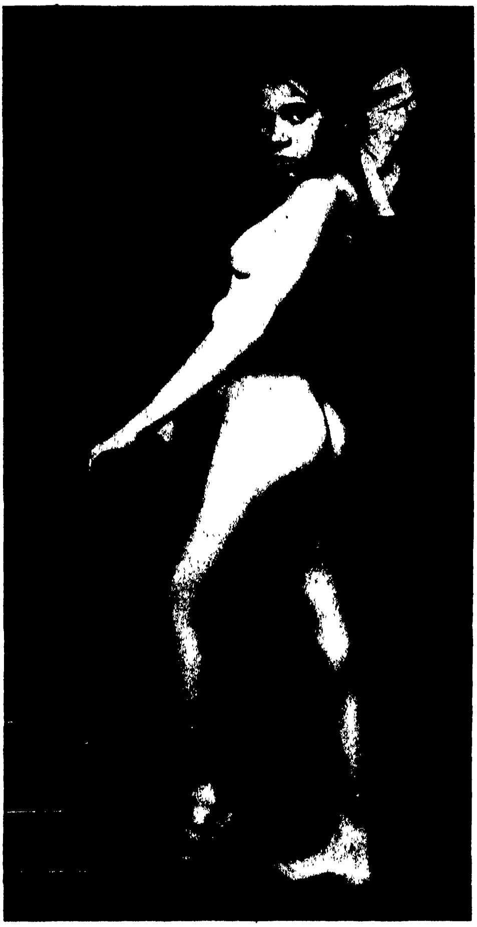


Fig. 48.—Hip Flexion Deformity. Poliomyelitis.

Treatment.—The **drainage** of these vesicles is usually followed by a very satisfactory relief from all joint inflammation. When the joint infection is purulent instead of serous or serofibrinous in form, thorough **drainage** and **washing out of the joint** is indicated, but even then the joint is apt to be destroyed. In this form of arthritis there is often very extensive destruction of the cartilage, followed by bony ankylosis. It is important to waste no time **in removing the original focus** when it can be located.

Joint Deformities

Deformities may be due to trauma, to static conditions, to muscu contracture, to muscle weakness, to atrophy, or to paralysis. Prena conditions and disease also cause deformity. When no disease remai or when the condition is not due to disease, the deformity should be corrected as early in life as possible.

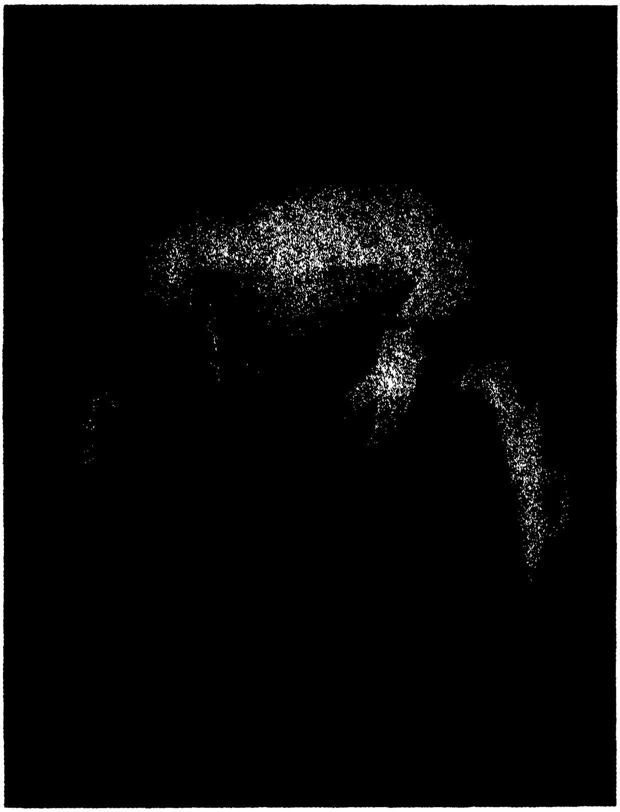


Fig. 49.—Coxa Vara.

Deformities of the Hip

Hip Flexion.—It is difficult and unsatisfactory to stretch the hip flexors when they are markedly short and when the hip has been held flexed for any length of time (Fig. 48).

TREATMENT.—Hip flexion, due to a pathological condition of the soft tissues, may be corrected by **operation** to lengthen the hip flexors (Soutter operation).

Hip flexion due to old disease or to fracture may be corrected by an oblique **osteotomy** just below the trochanter (Gant operation). The leg and pelvis should be held in an overcorrected position for six weeks. The results are very satisfactory.

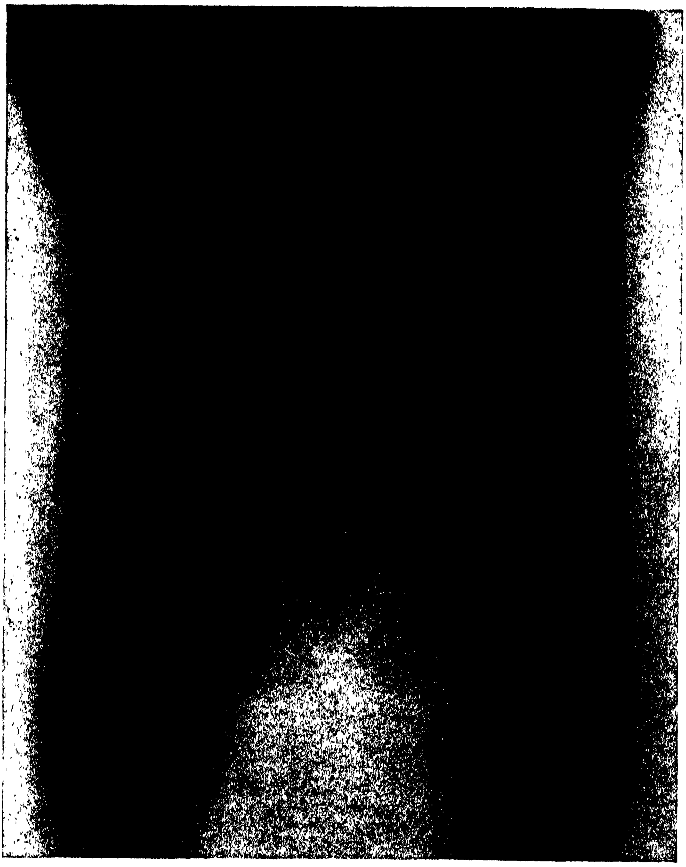


FIG. 50.—COXA VALGA.

Lordosis.—This deformity is often very painful and is frequently due to the stiffening of the hip in a flexed and adducted position. When this is the case the **deformity** should be **corrected** and the back will flatten and the pain be relieved. Occasionally lordosis is due to paralysis of some of the trunk-muscles, to faulty attitude in standing and sitting, to scoliosis, or to bony anomaly or deformity.

Coxa Vara.—Coxa vara consists in the decreasing of the angle of the neck of the femur, the head being lower than the top of the trochanter (Fig. 48). It may be due to fracture or to softening of the neck, as in rickets, and arthritis deformans. When a coxa vara exists the motion in abduction is more or less limited, depending upon the degree of the deformity. In extreme cases there is no motion in abduction.

TREATMENT.—Cases may be relieved entirely by an oblique **osteotomy** just below the great trochanter, the leg being placed in an abducted position, slightly hyperextended, and held there until the bone is solidly united. This takes from five to six weeks.

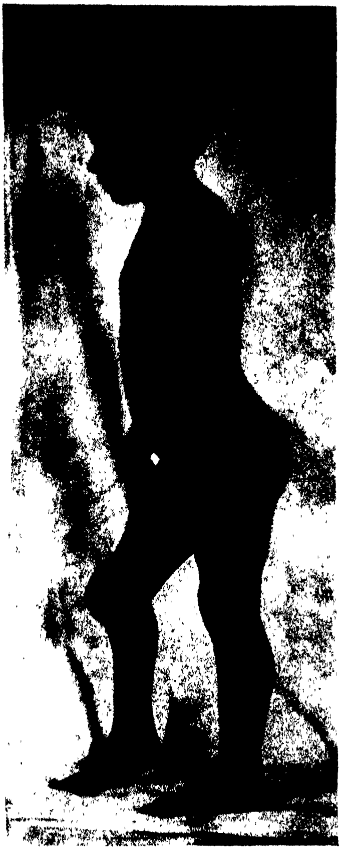


FIG. 51.—SUBLUXATION OF THE KNEE.

Coxa Valga.—Coxa valga is not as common as is the reverse deformity, coxa vara. The angle of the neck of the femur is increased, the head being higher than normal (Fig. 50). Usually the condition requires no treatment unless it accompanies a dislocation.

Deformity of the Knee

Knee-flexion.—TREATMENT.—Knee-flexion which has existed for any great length of time is often difficult to correct and can **rarely** be overcome by **manipulation.** A well-padded **plaster of Paris bandage** may be applied, and a slit cut in the plaster across the popliteal space. Small **wedges** are put in the slit, spreading the plaster apart. One or two pieces of wood one-eighth of an inch thick are added each day, or thinner ones if these cause pain. A flexed knee may be straightened in from three to six weeks in this way, the plaster being changed every five to ten days, depending upon the individual case. If this method is not successful, an **osteotomy** at the level of the adductor tubercle will allow the knee to be straightened and prevent the joint from being injured by the trauma of manipulation. After correction is established, a caliper

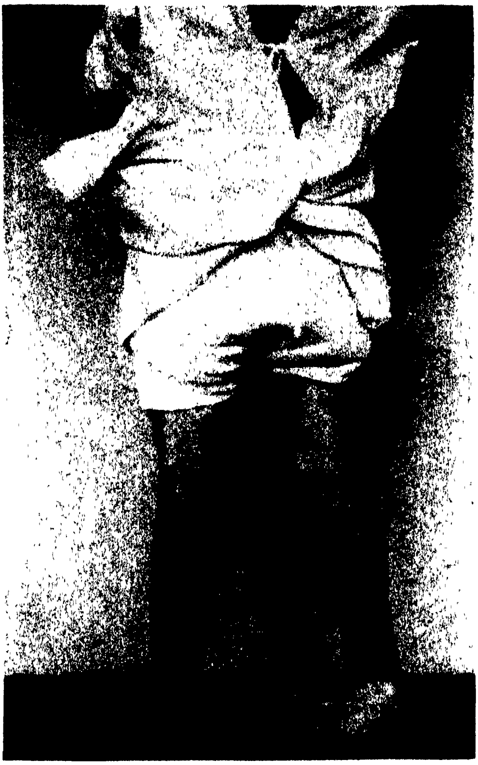


FIG. 52.—CONGENITAL CLUB-FOOT. (Equinovarus.)

splint is used for part of each day for from six to twelve months, depending upon the tendency to slight flexion.

Subluxation of the knee, depending upon the duration, is corrected by a **genuclast** (Fig. 51). If the joint action is good, it may be better to correct the flexion as described above, by an osteotomy, and not to attempt to correct the subluxation. The surgeon will have to decide in each individual case.

Deformities of the Ankle and Feet

Postural Conditions of the Feet.—ETIOLOGY.—Deformity is caused by a disproportion between the weight to be borne and the muscular power which bears it. Weakness of the muscles of the leg and feet caused by footwear which cramps the front of the foot, and by faulty attitudes in standing and walking, also weakness following trauma or illness, are the chief exciting causes.

SYMPTOMATOLOGY.—Deformity, pain, tenderness, muscular spasm, are noted. Stiffness and ungraceful gait are noted.

TREATMENT.—Relief may be obtained from the **replacement of displaced tarsal bones, removal of strains,** the overcoming of midtarsal stiffness and restoration of the muscular strength needed in sustaining the body weight, by means of **exercises,** and proper **shoes.**

Equinovarus (Club-foot)—Varus.—This is a deformity characterized by adduction of the front of the foot, depression of the front of the foot, and prominence of the cuboid bone. In extreme cases the patient walks on the cuboid and external malleolus, no weight being borne on the heel and sole of the foot (Fig. 52).

TREATMENT.—In infants, gentle **manipulation** may be begun about the eighth week and continued as the child grows older, if the deformity is considerable.

The deformity may be corrected by manipulation, by **tenotomies** and by manipulation, by **lengthening the ligaments** at the inner malleolus (Ober operation), by **removing a wedge of bone** and, in paralytic cases, by manipulation, tenotomies and **tendon transplantation** (Fig. 53).

In view of the better modern understanding of this deformity the **Phelps operation** for club-foot should be **avoided,** as the other operative measures are preferable.

Talipes varus is an inward twist of the front of the foot and prominence of the cuboid bone. When the foot is in an extreme varus position the plantar surface points to the side and the patient walks on the cuboid and malleolus.

Pes Cavus.—Pes cavus designates a hollow, contracted foot (Fig. 54). It may be inherited or may be due to high heels, or to excessive use of the calf muscles, as in the case of dancers, or to paralysis or muscle contracture.

The condition may be accompanied by some equinus and is probably due to a slight transient paralysis of the anterior groups of leg muscles and to contraction of the posterior group, or it may result from a sprain or fracture above the ankle. There are no symptoms, unless the equinus is exaggerated. The patient may require specially fitted shoes. There may be some pain and limitation of dorsal flexion, due to contraction of the plantar fascia.

TREATMENT.—Many **operations** have been suggested for this condition. If there is pain it is usually due to lack of dorsal motion of the foot, the equinus or to the claw-foot or hammer-toe condition. Pain will be relieved by the application of appropriate treatment for these deformities.

FIG. 53.—CLUB-FOOT. Postoperative position.

Equinus.—Equinus denotes a position of the foot with the ball of the foot pointing down. The patient is unable to reach the ground with his heel.

ETIOLOGY.—The condition is due to prolonged use of high heels, to faulty position following trauma, to prolonged bed treatment, or to muscle contracture, rheumatism, arthritis deformans, disease, inflammation or paralysis.

TREATMENT.—In certain anteroposterior flail conditions, when the displacement is lateral, and the muscles on the other side are normal, a muscle or tendon **transplantation** may be performed to balance the ankle. In some instances the insertion of **silk ligaments**, or **tendon fixation**, are advisable, in others, **astragalectomy**, with displacement of the foot backward may be preferable. This last operation in extreme flail conditions gives the most satisfactory results for weight-bearing without stiffness, and renders a brace unnecessary.

Deformities of the Wrist and Hand

Madelung's Deformity of the Wrist.—This is a subluxation of the wrist forward and generally toward the radial side. The ulna and radius are more widely separated than usual and the radius is usually curved. The condition is often bilateral.

ETIOLOGY.—The condition occurs usually in adolescence. The predisposing factors are relaxation of the ligaments, stretching of the muscles, previous rachitic deformity and sometimes injury.

SYMPTOMATOLOGY.—There is a weakness of the wrist, limitation of motion, chiefly of hyperextension, but sometimes also of pronation, and supination. Occasionally pain is present.

TREATMENT.—The treatment consists in **exercises, hyperextension, supports** and **massage**. Occasionally **osteotomy** of the radius is indicated, depending upon the amount of deformity and disability present.

Dupuytren's Contraction.—This is a deformity due to contraction of the palmar fascia, affecting also the fingers. These become flexed to a lesser or greater degree.

The *etiology* is not known. Arthritis, usually of the proliferative or degenerative type, is generally present to a greater or lesser degree in all cases.

The condition may be bilateral. There is thickening of the palmar fascia, or of the tendon-sheath or bone, and general contraction. Occasionally pain is present.

TREATMENT.—The treatment consists in multiple **incision** of the bands, or, if possible, complete **removal of the fascia**, followed by systematic and gentle **overstretching** in order to maintain the overcorrection obtained at the time of operation.

Congenital Club-hand.—There may be distortion in any direction. The condition may be due to constant pressure *in utero* without other abnormalities, or it may be associated with club-foot, absence of the radius or of the ulna (Fig. 56). The most important form is that associated with defective radius. In these cases the ulna is short and bent and often makes a right angle with the hand. There is also defective formation of muscles and ligaments. When there is absence of one of the long bones one or more fingers are absent on that side of the hand. Other deformities of the hand sometimes accompany club-hand, such as webbed fingers, deformity of the fingers or partly united fingers.

Treatment.—When no other deformity is present, **manipulation** and **fixation in plaster** may be sufficient. In other types, **tenotomies**, **tendon transplantation** and **osteotomies** are necessary, or, when one bone only is present, this is **split**, the carpal bones shaped to fit between, and in this way the hand is held straight so that the finger-tendons may function.

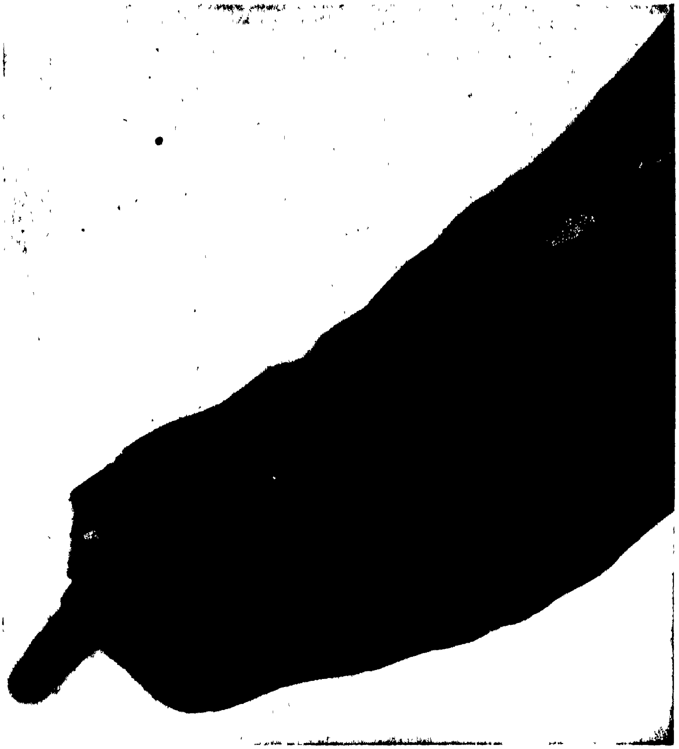


Fig. 56.—Club-hand with Absence of the Radius.

Other Pathological Conditions of the Joints

Limited Motion and Deformity of the Arms.—Treatment.—This condition is corrected by **manipulation** or **osteotomy**, and maintained in paralytic cases by **tendon transplantation** and **braces**. Knock-elbow is corrected by osteotomy, stiffness of the elbow by **plastic operation** on that joint. This will reëstablish the use of the joint, giving full **flexion** and extension to within 5 or 10 degrees of a straight line.

At the shoulder, a **partial excision** will help to correct the **limited** motion, provided the muscles are good.

Limited motion and stiffness of the wrist may be relieved by an excision. In rheumatic cases, operations for reëstablishing motion are not usually advisable.

Ankylosis.—This consists in the chronic fixation of a joint in a certain position. It may be a partial fixation, limiting the motion slightly or almost entirely, or it may be complete (Fig. 57). It is due to trauma, or to an inflammatory process within or without the joint, resulting in the formation of fibrous adhesions, or sometimes of bony adhesions, limiting the motion about the joint. The best way to prevent ankylosis is by proper treatment of the diseases of the joint, by **passive motion, baking** and **Bier's hyperemia treatment.** If ankylosis seems inevitable it should be changed to a position which gives the greatest function to the joint.

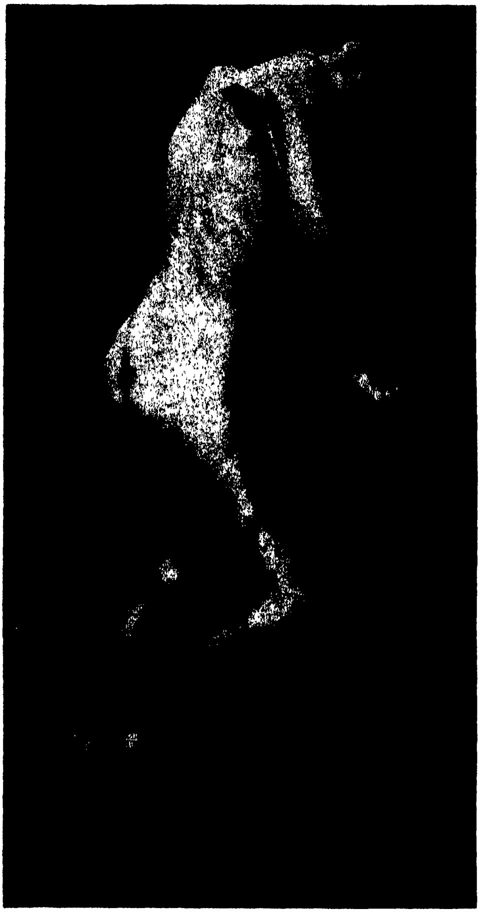


Fig. 57.—Ankylosis of the Hip.

Treatment.—Forcible **correction** is usually **inadvisable,** but the indications depend upon which joint is involved, and upon the type of ankylosis. Tuberculous joints should not be manipulated. After the disease is completely cured the limb may be straightened by an **osteotomy** done in the healthy bone above or below the site of the old disease. If the ankylosis is fibrous, repeated **manipulations** in recent cases are sometimes useful. If it is bony, osteotomy is indicated. When the ankylosis is due to trauma or to old disease, which has subsided long ago, but not to tuberculosis, **incision** or **arthroplasty** or other plastic operations are advisable in certain cases involving the shoulder, elbow, wrist, hip or ankle. The knee is not a favorable joint for arthroplasty.

Semilunar Cartilage Displacement.—This condition is usually traumatic, and the internal cartilage is the one most often involved.

Symptomatology.—The symptoms are sudden pain, inability to extend the leg fully, and swelling, with often a palpable protrusion of the cartilage. It is usually followed by a synovitis. One attack predisposes to succeeding attacks and in time the cartilage may be entirely loose and form a foreign body in the joint.

Treatment.—The immediate treatment consists in **reduction.** This is accomplished by flexing the leg as much as possible, by abduction of the femur, rotation inward and sudden extension. A **plaster of Paris cast** is used after the swelling has subsided. In chronic cases the treatment consists in **opening** the **joint** and removing the cartilage.

Relapses are often due to lack of recognition of the condition when it first occurs after the first attack, or to too short immobilization. It is important to allow time for the cartilage to adhere. When the swelling has subsided the plaster cast is continued and the patient allowed to walk, with a straight knee. **Immobilization** is continued for five weeks. Only slight motions in flexion are allowed for the following two weeks.

Prepatellar Bursitis (Housemaid's Knee).—This condition consists in an enlargement and an effusion into the bursa over the patella. The symptoms are pain, swelling, and discomfort in the region of the knee. The swelling is localized, and there is definite fluctuation. There may be suppuration. One attack predisposes to others.

Treatment.—The treatment consists of **counterirritation, hot applications, rest** and **fixation.** In severe cases the **sac** should be **excised.**

Loose Bodies in the Knee-joint (Joint-mice).—These may consist of bits of bone, cartilage, or fibrin. They are apt to be found in conjunction with synovial tuberculosis and arthritis deformans. They are freely movable, and cause no symptoms unless they become caught between the bony surfaces, in which case there is sudden, sharp pain followed by an effusion into the joint. The symptoms may recur.

Treatment.—The condition is treated by **removal of the loose bodies.** Whenever possible, they should be counted and located and the extent of the excursion of each body noted before operation.

Tenosynovitis.—Tenosynovitis of the wrist or tendo achillis is usually due to strain, to pressure, or to both. There is often exquisite tenderness and pain with motion, and loss of power.

TREATMENT.—In cases of long standing, mild **counterirritation, immobilization** and **protection** from all pressure on and in the neighborhood of the sheath are important. The shoe should be cut away behind for two inches at least, and loose leather used to cover the gap.

PATHOLOGY.—In some cases of long standing a few or many calcified deposits are found in the sheath. They may be small or large and long.

Acute Synovitis.—SYMPTOMATOLOGY.—The signs and symptoms are local heat, thickened capsule, fluid, spasm of the muscles, slight flexion of the knee, and limitation of motion.

TREATMENT.—The treatment should consist of **splints** or **plaster,** in the severe cases of the application of **ice bags.** Absorption of the fluid is favored by the use of the leg without the removal of the splint. When the condition is slight, **adhesive strapping** to limit the motion in flexion is of value, with **rest** for from three to five days, followed by the use of the leg without removal of the adhesive bandage. **Rubber anklets, knee-caps, wristlets** and **elbow supporters** are apt to interfere with the circulation and repair. Where it is necessary to use them, they should be discontinued as soon as possible. **Exercises** and **massage** are indicated after the acute symptoms have subsided.

Intermittent Synovitis with Effusion.—The condition exists without apparent cause, occurring at regular intervals every two, three or four weeks. There is discomfort and swelling, which disappears after from three to five days. Digestive disturbances sometimes accompany the condition. It is probably a trophic neurosis.

TREATMENT.—The treatment consists of general hygiene, regular **exercises** and **habits** of life, **care** of the **bowels** and digestion, and the administration of **thymus extract.**

Charcot's Disease.—ETIOLOGY.—This form of joint disease may be associated with locomotor ataxia, syringomyelia, Pott's disease, acute myelitis, injuries of the peripheral nerves, etc. The joints are usually affected in the following order: knee, hip, shoulder, tarsus, elbow, ankle, wrist, jaw and spine.

SYMPTOMATOLOGY.—This condition occurs in syphilitic and tabetic patients. There is a degeneration of the cartilage and of the underlying bone, with irregular formation of cartilage about the joint. Thickening of the synovial membrane takes place. With the condition there is often a looseness about the joint, the knee, hip or ankle. There is marked swelling and effusion and often considerable deformity. No local pain nor sensitiveness are noted. There is usually more or less weakness. The process often progresses until there is actual dislocation.

TREATMENT.—Very often no treatment is necessary when the condition is slight, but in the case of the joints of the leg, **apparatus** is often necessary to support the joint and prevent dislocation.

PATHOLOGY.—The pathology is much the same as that found in arthritis deformans. The activity of formation is less, while the destructive process becomes very rapid.

Gout.—SYMPTOMATOLOGY.—Patients with gout come to the orthopedic surgeon because of the pain and swelling about the joints. It is a

medical disease. There are acute inflammatory processes with chronic changes about the joints, and characteristic deposits of sodium urate in the cartilage surrounding them. Before the joints are enlarged there may be infrequent twinges of pain. An *x*-ray will often show a thinning of the middle of the shaft of the metacarpal or metatarsal bones early in the condition (Fig. 58). The pain first appears in the feet and hands, especially in the great toe joints. These are hot and tender, and an irregular deformity of the small joints occurs. There may be three or four severe attacks a year and sinuses may develop at the joints.

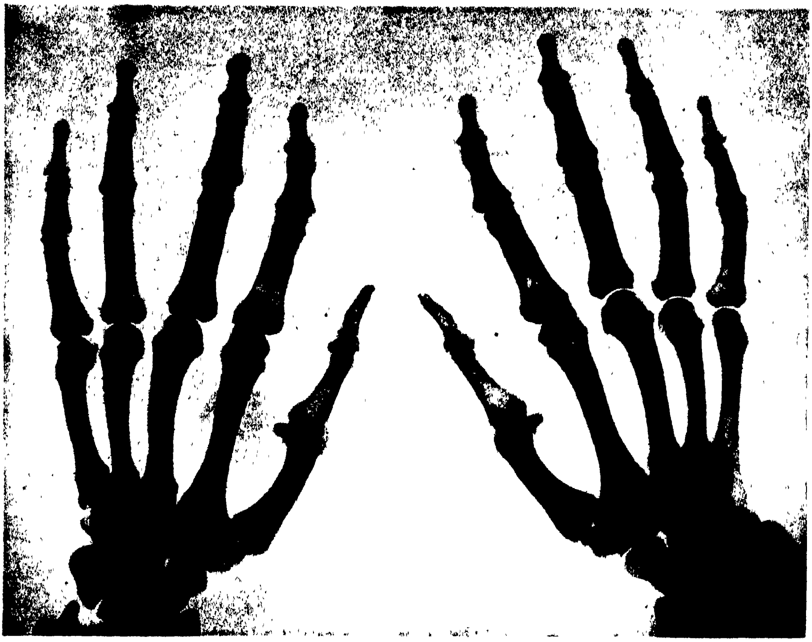


FIG. 58.—GOUT. The thinning of the proximal phalanges is shown near their distal ends.

TREATMENT.—Treatment consists in **rest in bed, warm applications** and **soaks** to allay the inflammation. **Cold** is sometimes more acceptable than heat. Digestive symptoms should be treated. Doses of **calcium** and **salicylate** will help to relieve the pain. Eight or nine glasses of **liquids** should be taken daily.

Scapula Crepitus.—Scapula crepitus is the name applied to the condition of grating produced by motions of the scapula. The affected side is usually tender at certain points. There is, as a rule, a small bursa or gland, or a dry condition of the muscle. Bony irregularities are sometimes present.

TREATMENT.—When there is much pain, **heat, gentle massage** and **exercises** will relieve the pain. In some instances **immobilization** is necessary.

Sprained Ankle.—A sprain of the ankle is generally caused by suddenly turning the foot inward or outward with sufficient force to cause injury. The injury may consist in the stretching or rupture of tendons, tendon-sheaths, capsules, muscle-fibers, in conjunction with injury to the synovial membrane. There may be effusion or hemorrhage into the joint. An *x*-ray photograph should always be taken, in order to exclude the suspicion of fracture.

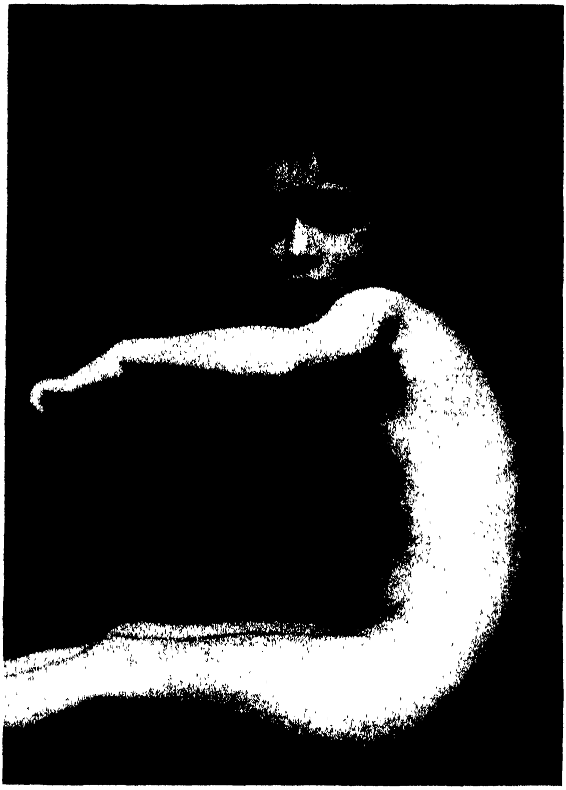


FIG. 59.—ISCHEMIC PARALYSIS.

SYMPTOMATOLOGY.—The symptoms are severe pain, throbbing, swelling, heat and sometimes discoloration.

TREATMENT.—The treatment consists in **immobilization** and **rest** with **adhesive strapping** or, in severe cases, in the adjustment of a **light plaster** with the foot in slight dorsal flexion.

Subdeltoid Bursitis.—There is sometimes an inflammation of the bursa lying underneath the deltoid muscles.

SYMPTOMATOLOGY.—The symptoms are pain, tenderness, and limited motion, chiefly in abduction and rotation. Sudden motions are accompanied by sudden, sharp pain. There is no involvement of the joint. Gradually an atrophy of the shoulder-muscles results. The cause is often trauma, but at other times the etiology is obscure.

TREATMENT.—The treatment in the acute stage includes **rest, heat** and **counterirritation,** and **fixation.** Later **massage** and **graduated exercises** are indicated. In obstinate cases **operation** for the **removal of the bursa** is sometimes necessary.

Ischemic Paralysis—Contraction.—This condition is observed following the application of apparatus for fractures about the elbow. There is prolonged constriction, due to the pressure of the apparatus. This results in swelling, discoloration, numbness, and later paralysis and contracture (Fig. 59). There is fibrous degeneration of the flexor muscles resisting extension. The fingers and wrist are flexed and sensation is often lost.

TREATMENT.—**Prevention** of the deformity is important in fractures of the elbow. The apparatus should be frequently examined and the patient should move the fingers early in the treatment.

When paralysis occurs the fingers and hand should be put in **hyperextension. Exercises** and **massage** should be started as early as possible. The contractures have been relieved in some cases by **shortening of the bones** of the forearm, followed by **muscle-reduction.**

SECTION VII

DISEASES OF THE MUSCLES

CHAPTER I

INFLAMMATORY DISEASE OF THE SKELETAL MUSCLES

By C. F. Hoover, M.D.

Etiology, p. 527—Symptomatology, p. 528—Differential diagnosis, p. 528.

Muscular rheumatism, p. 530:—Symptomatology, p. 530—Dermatomyositis, p. 536:—Etiology, p. 536; Symptomatology, p. 536; Treatment, p. 541; Pathology, p. 542—Gout, p. 543—Myositis fibrosa, p. 543—Syphilitic myositis, p. 544—Trichinosis, p. 545—Gonorrheal myositis, p. 545—Muscular atrophy and joint diseases, p. 545.

Literature on disease of the skeletal muscles is not abundant. If we consider the volume of the muscles, their function, blood supply, and exposure to injury from external and internal sources, we find the attention given the muscles in both clinical and pathological literature to be very meager. In fact, the physician is prone to neglect the consideration of the skeletal muscles. There seems to be a general assumption that muscles are immune from disease. This criticism is based upon the common failure to consider the abdominal muscles in patients who complain of abdominal pain, upon neglect of the neck and shoulder girth muscles when the patient complains of pain in this region; and also upon neglect of the lumbar and pelvic girth muscles when the complaint is of pain in the sacrolumbar and hip region.

Etiology.—On account of the free anastomosis of blood-vessels, there are not many instances of gross lesions of the muscles from ischemia and infarcts, although in the absence of a proper examination small infarcts of the muscles may escape attention. Metastatic infections of the muscles are commonly located near the junction of the muscle with its tendon or aponeurosis, and for this reason a disease of the muscle may be mistaken for disease of a neighboring joint or tendon sheath. Joints, ligaments, tendons, and bursæ are much more frequent sites of disease than are the muscles, and on account of the predominance of these sources of pain, the muscles are quite neglected. Subjective pain from a muscle is not located with the same accuracy as is pain in superficial structures. Consequently the vague location may be very misleading, and unless the muscles of the affected area are carefully examined, the pain is likely to be interpreted as originating from a nervous source.

Symptomatology.—EXAMINATION OF A MUSCLE.—There is nothing new to suggest in the examination of a muscle, except one point which has not been noted in any literature on the subject. Observations without comment have been made by several writers to the effect that patients suffering from several forms of myositis experienced little discomfort in walking, but that the muscles were painful to pressure and were very painful when they were stretched. One of the author's patients ruptured eight muscles in myositis of prolonged duration, but suffered very little pain when the ruptures occurred; he stated that there was little pain preceding the ruptures.

Unlike most other structures which are tested for the seat of pain, functional employment of a muscle is painless when the seat of the disease lies within the muscular sheath. Perimyositis may cause pain when the muscle is activated, but myositis causes pain only when the part is palpated or when the muscle is stretched. If this point is neglected, myositis will be overlooked. It is the general practice to employ a structure functionally, as a test for pain; if exercise of the normal function is painless, the suspected structure is eliminated as a source of pain. It is distortion of the affected area which causes pain when pressure is applied. If it is applied equally in all directions, as hydrostatic or pneumatic pressure is transmitted, it will not cause pain. This is the case when a muscle is activated. The contents of the muscle-sheath constitute a semi-liquid mass, and when the muscle is contracted there is an increase of intramuscular pressure; but the pressure is equally transmitted in all directions, and causes no distortion when an inflamed area occupies a small part of the muscle, nor when it extends throughout the muscle, as in some cases of trichinosis. When pressure is applied to an area of myositis, or when the muscle is stretched, there is distortion of the affected area, so that the conditions are attended by severe pain. If stretching a muscle causes pain, it should be carefully palpated for sensitive areas and for palpable welts or nodules.

Differential Diagnosis.—It is true that a differential diagnosis of gout, rheumatism, exposure to cold and moisture, and other sources of metastatic infection of the muscle, is very unsatisfactory. Very often one cannot palpate any swelling or area of induration in the muscle, but the point of sharply defined tenderness can be very clearly located, and by the employment of several tests for the location of intramuscular disease the muscle may be satisfactorily proved to be the source of pain, although the etiology of the painful point often remains in doubt.

A woman, about fifty years of age, was recently admitted to the wards at Lakeside Hospital, suffering from a painful affection of the upper right abdomen, on account of which surgical exploration of the abdomen had been advised. It was for this reason that she came to the hospital for further advice. The secretory and motor functions of the stomach were found to be perfectly normal, and there was nothing in the history nor in the findings which indicated that the gall-bladder or the gall-duct was at fault. The patient complained of pain, which she described as being vaguely located over the upper right half of the abdomen. On palpation a point was discovered in the external half of the right rectus muscle, on a level with the seventh costal cartilage, which was exquisitely sensitive to pressure. If this point was palpated when the muscles were activated, the tenderness was greater than was the case when the muscles were relaxed. The tender area was not larger than the berry of a man's thumb. There was no palpable induration or swelling. If the patient made an effort to sit up, no pain attended the effort. However, when a firm bolster was placed under the small of her back so that she was put into the position of lordosis, and the rectus abdominis was stretched, she complained of severe pain, which was referred to the upper right abdomen.

When a painful point is located in the abdominal muscles, and differentiation between the abdominal muscle and the abdominal peritoneum is to be made, tests of pallesthesia and perception of cold may be employed in making the differentiation. For instance, as in the case just described, if the palpably located tenderness has originated from localized peritonitis in the abdominal wall, one will find a small area over the site of the tenderness, perhaps not more than an inch square, over which the vibration of the tuning-fork will be much less keenly perceived than over a point on the symmetrically opposite side of the abdomen. Over this same area the perception of cold will also be greatly diminished. It is common to find over these areas complete loss of perception of the vibrations of the tuning-fork; in such cases even intense cold may not be perceived as cold. This area of dissociation of sensory percepts is not consistent with the distribution of the peripheral nerves, nor does it have any relation to segmental distribution from the spinal cord. The area is palpably defined and palpably located as the site of underlying peritoneal irritation. This dissociation of sensory percepts in the skin overlying an area of peritoneal irritation is of service in locating the site of an intra-abdominal source of pain when disturbances of the adnexa, appendix or gall-bladder, ulcer of the stomach, or invasion of any other circumscribed area of the peritoneum accompanies a lesion. The writer has always found that, when localized tenderness can be demonstrated within the abdominal muscles, the impairment of pallesthesia and perception of cold are not disturbed.

On several occasions the writer has seen patients with localized tender spots at the right of the rectus abdominis, over the site of the appendix. The tenderness on palpation was exquisite; the patients complained of the pain but were just as vague as to its location as most patients are who have pain from an intra-abdominal source. Several of these patients were rheumatic. One of the cases occurred during the recent epidemic of influenza, and during army service in France 2 cases of this character were found among trench fever patients. In all these instances the question of appendicitis was raised, but it was possible, by asking the patient to contract the abdominal walls, to prove the tenderness to be in the abdominal wall and not in the abdominal cavity. Activation of the abdominal muscles was painless. Pressure on the sensitive area caused more pain when the muscles were activated than when they were relaxed. When the muscles were stretched the pain was severe.

Muscular Rheumatism.—This term is commonly treated with disdain by physicians, but is much used by the laity to describe their painful symptoms. The real truth lies somewhere between these extremes. The 2 cases described below are unusual on account of the severe muscular lesions, but they served the purpose of arousing the writer's interest in muscular lesions accompanying rheumatic arthritis, and as a result a number of cases of lesser severity were subsequently found which would certainly have been missed had not the severe examples been encountered.

SYMPTOMATOLOGY.—A woman, thirty-eight years of age, came to Lakeside Hospital in January, 1916. The patient dated her illness from an attack of "grip" six weeks before her entrance to the hospital. She had at that time been confined to her bed for two weeks. She had also suffered from cough, general malaise, sore throat and some joint pains. After recovery from her "grip," the patient began to have pain in the extremities and also in the vicinity of the jaw. She was unable to open her mouth on account of "pain in her jaw." The pains in her legs were rather indefinite in character, but she said that they started from the hips and went down even to the soles of her feet. In the arms the pain was mostly in the upper portion, but there was also some pain about the wrist, and the patient complained of inability to raise her arms above her shoulders in combing her hair.

When the patient was admitted to the hospital, she had an evening temperature of 100° F. (37.77° C.), with a pulse-rate between 70 and 80. There was no evidence of any involvement of the heart, or of the veins or arteries, and she was free from any demonstrable arthritis. Examination showed that the masseter muscles on both sides were very sensitive to touch. The right was distinctly more tender and thicker than the left. The floor of the mouth, and the muscles which move the tongue, were not involved, nor were the temporal muscles. The patient was able to bite without pain, but when she attempted to open her mouth, the movement was attended by very severe pain, which she referred to the temporomaxillary area. The pain could be definitely connected with passive stretching of the masseter muscle. The right triceps muscle in its lower half was distinctly indurated and sensitive, although the muscle was not paretic. Strong flexion of the forearm on the right side caused severe pain, which was located in the lower portion of the triceps. The right abductor indicis was indurated throughout its entire extent and exquisitely sensitive to touch. None of the neighboring muscles of the thenar eminence were involved. Activation of the muscle caused only slight pain, but stretching of the muscle was exquisitely painful. All the intercostal and abdominal muscles were normal. The adductor magnus on the right side was palpable as a thickened mass from its origin at the ramus of the pubis to its insertion. It was painful on pressure and traction, but activation was not painful. In the plantar aspect of the right foot, over the adductor hallucis and over the flexor brevis digitorum and the flexor longus hallucis tendon, the area was sensitive to pressure and the muscles were sensitive to stretching. There was shortening of the flexor longus hallucis, so that the terminal phalanx of the toe was flexed, producing hammer-toe. This abnormality the patient said was due to an old process, quite similar to the present attack, which occurred five years ago. The flexor longus hallucis was not as painful as the other muscles. In the mid-portion of the belly of the right quadriceps extensor was an indurated area about three fingers in breadth which occupied the entire breadth of the muscle. This area was painful to pressure and when stretched, but active extension of the leg by the quadriceps was not painful. Over the right peroneal tendon, directly over the external malleolus, was a small nodular mass, about the size of an average peanut kernel, which was indurated and tender and felt like bone. It was apparently situated in the tendon-sheath. It was apparent at the upper border of the external annular ligament, and marked the portion of the belly of the peroneus tertius muscle where it joins the tendon. Plantar flexion of the tarsus caused extreme pain even with the toes in full extension.

From the clinical history of this patient, it could be definitely determined that she had had a joint inflammation during her first attack five years before, and it seemed very probable that we were dealing with a Payne-Poynton infection, although this point could be established only on the basis of clinical interpretation. There was no bacteriological evidence as to the character of the infection.

The second case of rheumatic myositis was in a man thirty-three years of age, who came to Lakeside Hospital in February, 1916. His illness had begun about fifteen years before while he was at school. He was seized with pain and swelling in his hands, knees and feet, and was forced to go home. This illness, which had such an acute onset, confined him to the house for about three years with arthritis. He said that during that time he had felt perfectly well with the exception of the pain in his joints. He also stated that nodules sometimes appeared about certain joints and under the skin of his legs. They would become quite sore and then entirely disappear. About thirteen years ago he lost the extensor power of both thumbs and of the third finger on both hands. The patient stated that this loss of power came on very suddenly and suggested the rupture of a muscle or tendon. Two years ago the extensor power of his legs was temporarily lost. This occurred suddenly when he attempted to run.

Physical Findings.—The joints of the upper extremities were normal; there was no resistance or pain on motion; no atrophy was present in the arms, but in both hands the interossei were atrophied, and the wrist joints and metacarpal phalangeal joints showed some thickened remains of former inflammation. The extensor power of the proximal and terminal phalanges of both thumbs was gone. The extensor power

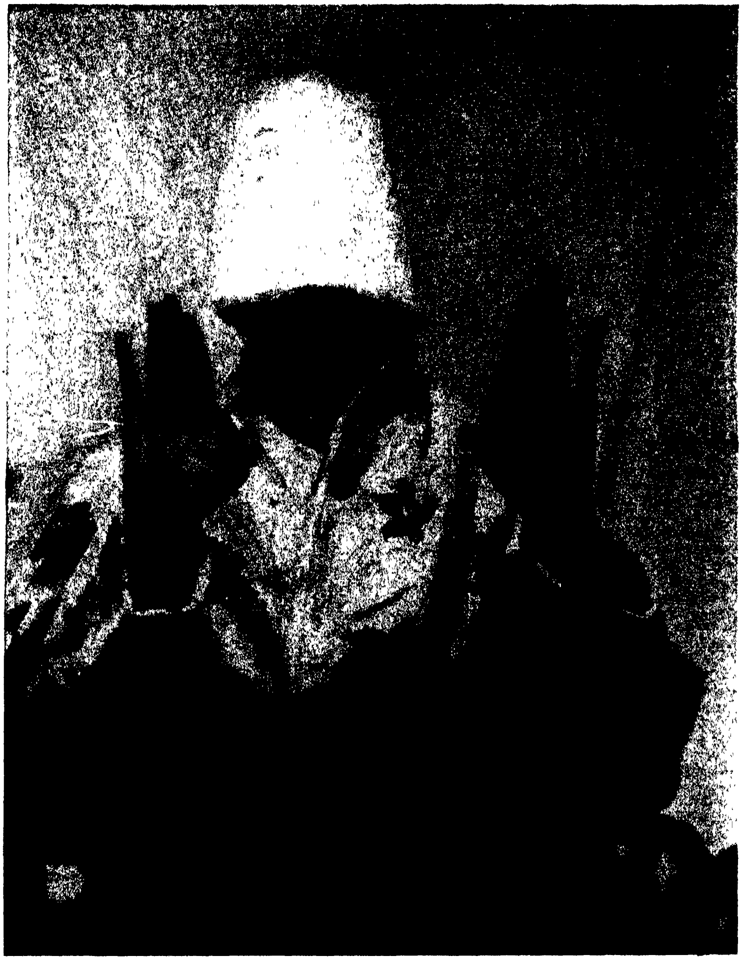


FIG. 1.—MUSCULAR RHEUMATISM. In this picture the patient was asked to hold his fingers and thumbs in an extended position. The photograph shows how the metacarpals of the thumbs are extended; the first and second phalanges remain in a partially flexed position. Both ring fingers are also in a partially flexed position at the metacarpal phalangeal joint.

was preserved in the metacarpal of both thumbs, but, as shown in the accompanying photograph (Fig. 1), there was a complete loss of extension of the phalanges. In the lower extremities, as the photograph (Fig. 2) reveals, there was a fibrous strand in the lower third of both quadriceps extensors. This fibrous strand marks the position of a rupture of the quadriceps muscles, which occurred two years previously with moderate exercise. The photograph reveals the prominence at the lower end of the proximal portion of both quadriceps muscles. There was also a palpable induration in the muscle in the lower third of the leg. The patient says that formerly there was marked thickening and tenderness at this site. The induration was bilateral, and on the right side the muscle could be identified as the extensor propius hallucis.

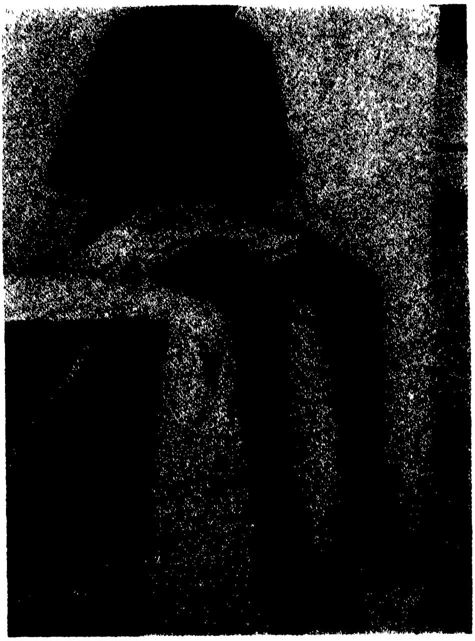


FIG. 2.—MUSCULAR RHEUMATISM. This picture shows the diminution in volume of the leg muscles, and the smooth, indurated and bronzed skin; the same characteristics of the skin and muscles of the forearm are apparent.

The accompanying photograph of the cervical region (Fig. 3) shows a prominence of the sternocleidomastoid muscle on the left side. This prominence was due to a fibrosis and consequent shortening of the lower third of the muscle, which was diseased during the first attack, fifteen years ago. For the present the disease has left fibrosis and shortening of the sternocleidomastoid of the left side, loss of power and extension of both phalanges of both thumbs, and the loss of the extensor power of the proximal phalanx of both right fingers. There was a fibrous union following the rupture of both quadriceps extensor

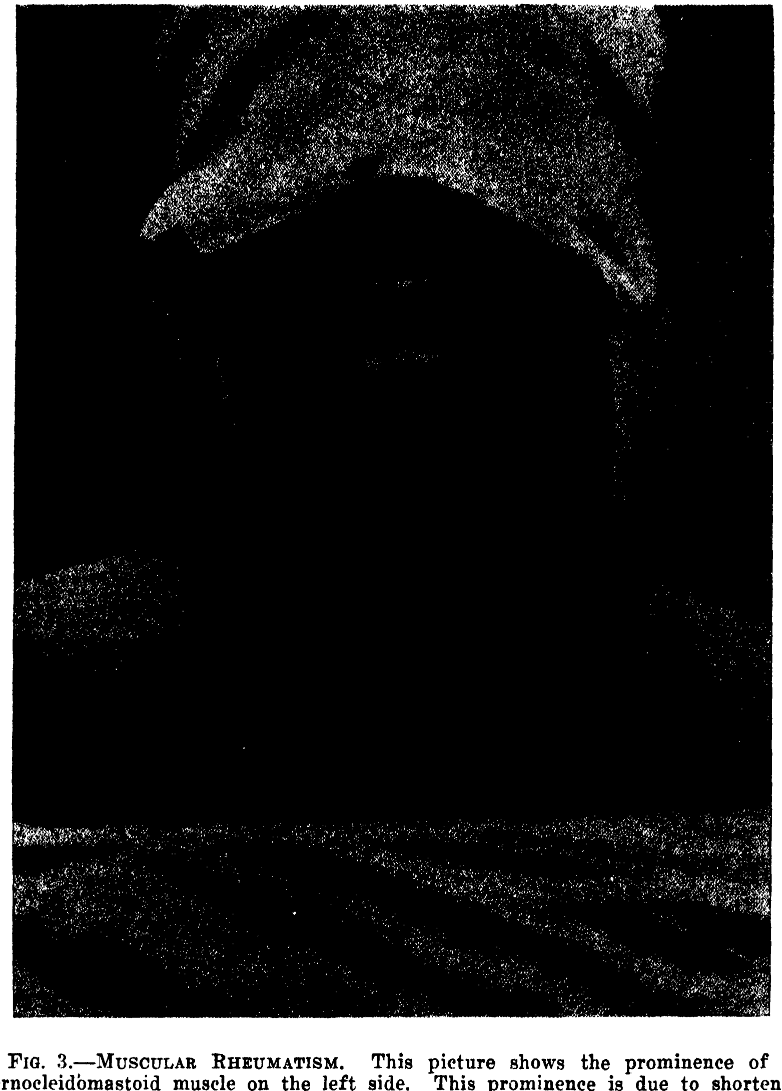


FIG. 3.—MUSCULAR RHEUMATISM. This picture shows the prominence of the sternocleidomastoid muscle on the left side. This prominence is due to shortening of the muscle from fibrous degeneration in its lower third.

muscles, and fibrous induration of the propius hallucis muscles of both sides.

In addition to the history of arthritis and the remains of extensive muscular disease which was incurred coincidently with the arthritis, the patient had traces of an old endocarditis, which left him with

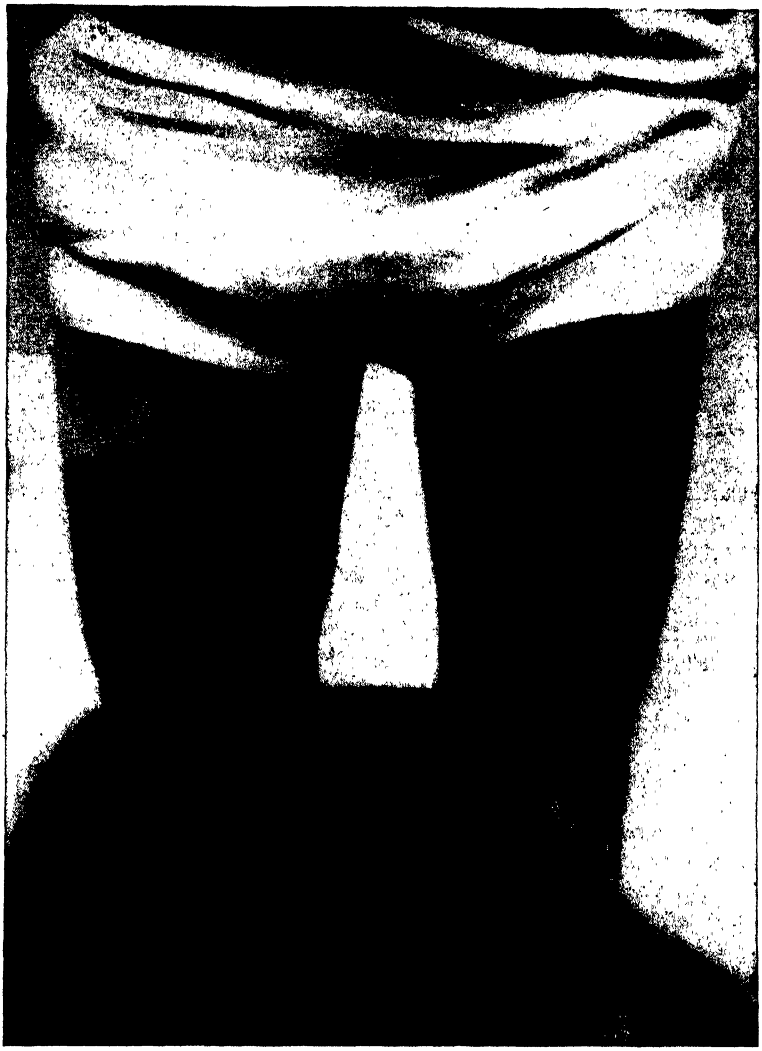


Fig. 4.—The patient is standing erect, and was told to activate both quadriceps muscles. The eminences at the middle of both thighs mark the locations of the proximal ends of the ruptured quadriceps muscles.

enlargement of the left and right ventricles. A loud blowing murmur could be heard during systole over the apex, which was interpreted as the result of an old mitral endocarditis.

These 2 cases bring out several characteristic features. In both instances there was disease of the body of the muscle, and in one case the disease was so extensive that a number of skeletal muscles were ruptured by slight violence (Fig. 4). In both instances the muscular disease accompanied an acute arthritis, and in the first case all pain was associated with passive stretching of the muscle, and not with activation. In both cases there was not only decided evidence of disease of the belly of the muscles, but there was a want of evidence of disease in the perimuscular structures.

Dermatomyositis.—In 1887 Unverricht[1] described a case which he named *perimyositis acuta.* The patient was a young man who had acute inflammation, edema, and tenderness of many skeletal muscles, viz., the extensors, the vasti of the thigh, and the muscles of the back and neck. The laryngeal and pharyngeal muscles, the diaphragm, and the eye-muscles were free. Unverricht emphasized this fact as evidence against the possibility that the case was one of trichinosis, and at the autopsy a careful search for trichinæ proved negative.

ETIOLOGY.—Unverricht says in the article mentioned above that we are coming to recognize that acute inflammation and degeneration of the muscles may occur without lesions of the anterior horns of the gray matter of the spinal cord, contrary to the view of Charcot, which had dominated the field up to that time. Unverricht believed that his case was one of rheumatic infection, and although he attached no importance to the fact, he stated that traction on the muscles caused pain, whereas the patient was able to walk with only moderate discomfort.

SYMPTOMATOLOGY.—In a later publication a case of dermatomyositis is described by Unverricht as beginning with fever, splenic swelling, edema, erythema of the skin, urticaria, and infiltrating nodules. Ultimately the muscles of swallowing may be involved, and also the intercostals, but the muscles of the eye, heart, tongue, and diaphragm escape. The patients ultimately succumb to suffocation, with pulmonary disease. Dermatomyositis is a good term, and there is no adequate reason for suspecting that disease of the peripheral nerves is the original lesion. The atrophic muscles do not show signs of the reaction of degeneration. The skin may show erythema or measles-like eruptions, which disappear, leaving only brown pigments behind. Hemorrhage into the skin and into the intestine have occurred in some cases, but can be explained only on the basis of a constitutional infection. Muscles have been found in all stages of degeneration. The fibrillæ have been seen to be differently involved. In some instances the entire length was swollen, with hyalin and fatty degeneration. There were also transverse lesions, as well as lesions involving the entire length.

The shortest duration of any reported case was eight days, and four months is about the longest duration of any of the acute fatal cases. The pathologic picture of the disease is essentially a perimyositis and infiltration of the muscles with interstitial exudation. There is some question as to whether or not the massive disease of the muscles is not secondary to the intermuscular inflammation. A bacteriological solution of dermatomyositis is thus far wanting.

Clinical History.—Only 3 instances of dermatomyositis have come under the writer's observations. The first of these occurred in the case of a negro, twenty-six years of age. This man had noticed for nearly three years prior to his entrance to the hospital that his hands and feet were swollen when he rose in the morning, and about one year before entrance there was swelling, redness and tenderness of the ankles, knees, wrists, and shoulders, with fever. Nine months before entrance the patient noticed that his calves were becoming stiff and that the skin felt tough. During the previous year he had been considerably embarrassed by what he described as a hide-bound condition of his skin, which did not permit free movements in the ankles, forearms and shoulders, and also impaired the movements of the muscles of his face. The skin was smooth and glossy, and both skin and subcutaneous tissue were hard and tough. There was a lack of the normal oil of the skin, and no sweat. One could not pick up the skin in folds anywhere on the body except about the genitalia. There was no normal glide of the muscles under the skin; skin and muscle moved together. When one palpated over the tendon-sheaths and over the muscles during motion, a definite crepitation was felt, similar to the creaking of a Russia leather binding, and a grating was felt when the muscles were passively moved. There was no muscular atrophy or sign of any old arthritis. The patellar reflexes were normal in degree and promptness. The man was unable to move the upper arm above the horizontal position, owing to restraint of his latissimus dorsi and pectoralis major. The involvement of the masseter muscles could be plainly palpated. The mouth could be only partly opened on account of the impaired extensibility of the masseters. On attempting to elicit electrical reactions in the forearm and leg-muscles, it was found that there was no sign of reaction of degeneration.

This patient remained in the hospital for about eight weeks, and at the end of that time left in about the same condition in which he had entered. During the entire time there was no elevation in temperature nor acute involvement of any joints.

The second instance of dermatomyositis to come under the writer's observation was the case of a man, fifty years of age, who entered the City Hospital in Cleveland on account of exhaustion and very distressing paresthesia, which he referred to both legs and feet. The man had cardiac enlargement, with the apex in the sixth interspace one inch outside the nipple line. There were no evidences of any valvular disease or of any disease of the aorta or peripheral vessels. The arterial pressure was 135/90. There was very moderate edema of the back of the neck and of the skin of the entire trunk and thighs. The edema was due to an acute nephritis. The urine contained an abundance of albumin, hyaline and granular casts, leukocytes, and a few red-cells. There were very marked evidences of dermatomyositis in both legs and feet and in the vicinity of the neck and shoulders. The skin from the knees down to the toes had about a normal thickness but was of a parchment-like consistency, with intense bronzing over the affected area. The skin could not be wrinkled into folds, and was attached to the underlying tissues. There was no crepitation, for the fixation seemed too firm to admit of sufficient gliding of the skin to cause crepitation. The muscles of the calf of the leg were much diminished in size, and greatly increased in consistency, and so inelastic that dorsal flexion of the tarsus was prevented. When the patient stood upright, he could not raise the ends of the metatarsals from the floor. He could raise himself on his toes about half the normal distance. Passive plantar and dorsal flexion of the tarsus was very much hindered by the inelasticity of the muscles and of the underlying skin and fascia. The muscles were not sensitive to pressure, nor were they sensitive to traction or activation.

The patient was a Slav, with whom the author had great difficulty in communicating, but so far as could be learned from the man, there were no abnormal responses to any kind of test for the sensory percepts. All the arteries in the feet and legs were normal, and it seemed that the paresthesias from which he suffered could be traced to involvement of the peripheral nerves secondary to fibrosis of the skin and fascia. On the back of the neck the skin was thicker than normal, markedly indurated and deeply bronzed. Activation, traction, and pressure caused no pain so far as the muscles of the neck were concerned, but there was marked limitation in the anteroposterior and lateral flexion of the head on the trunk. The limitation in the neck muscles was due to the same process that limited the movement in the muscles of the leg and feet.

How long the dermatomyositis had existed in this man, it was impossible to learn. He seemed to have given little attention to it. The only thing that disturbed him was the paresthesia in his feet and legs, and he was led to seek relief at the hospital on account of progressive weakness attending his myocardial lesion, and nephritis. The author could find no evidences to explain the etiology of the process, but it seems to have been a case of dermatomyositis which was limited in extent and had reached a permanent stage. The only symptom of which the patient complained was the paresthesia, which seems to have been evidence of a secondary involvement of the peripheral nerves.

The third patient with dermatomyositis was a boy seventeen years old, who entered Lakeside Hospital in August, 1920. This patient had very extensive induration of nearly all the muscles of the face, neck, trunk, and extremities. The volume of the muscles in this instance seemed to be very well preserved. They were not painful, but they were indurated and had lost their normal capacity for extension, so that the rigidity of the muscles was responsible for the limitations of movement. The dermatitis was very much less in extent than in the two preceding cases. The skin was thin, had a parchment-like texture, and was intensely bronzed, but there was not the same fixation of the skin to the underlying muscles as was described in the preceding cases.

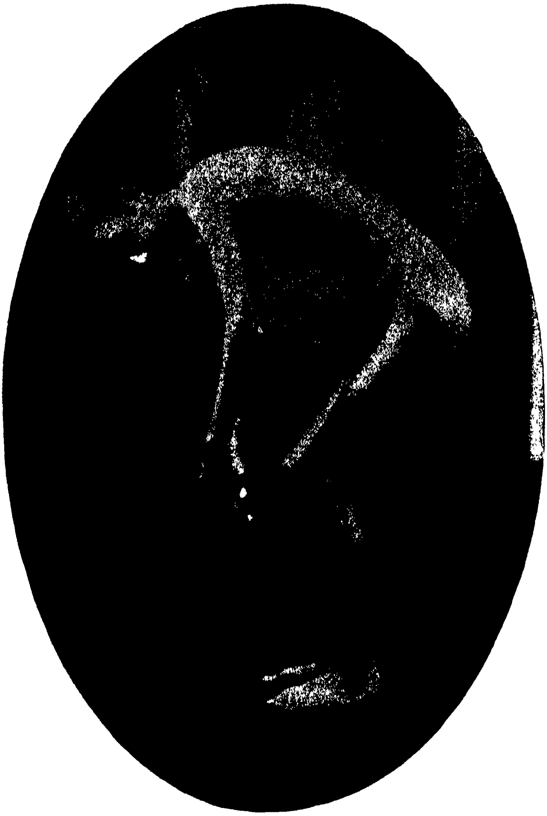


FIG. 5.—The patient is trying to flex the head on the trunk, to throw the arms in the horizontal position, to bend the trunk on the thighs, and also to bend his knees.

The patient was not hide-bound, but he was muscle-bound. Besides these changes in the muscles and skin, there was some evidence of tenosynovitis located over the dorsal aspect of the wrists in the long extensor tendons of the fingers. The only clear evidences of a former arthritis were in the wrist joints. *X*-ray examinations were made of the bones and the note made that they were "thin and fragile."

Of the two accompanying photographs, Fig. 5 shows the patient when directed to bend his head downward. He was also to throw his arms into as nearly the horizontal position as possible, and he is trying to bend the trunk on his thighs and to bend his knees, with the clearly depicted results. In photograph Fig. 6, the patient was instructed to straighten his arms at the elbow, to elevate them as high as he could, and also to bend backward and throw his head backward. The results of this effort, as shown in the photograph, very clearly depict the rigidity of all the muscles of the arm and thoraco-scapular and humeral muscles, also the rigidity of the anterior flexors of the head, and of the recti abdominalis and the flexor iliofemoral muscles.

Fig. 6.—The patient is trying to bend the head backward, to throw the arms upward, and to bend the trunk backward on the hips.

The literature on the histology of myositis is all very much the same, and gives rise to the suspicion that one of the basic difficulties lies in the fact that the histology of the normal muscle, in its relation to postmortem time, and method of hardening and of staining, has not been satisfactorily worked out. Saltykow[2] injected calomel, turpentine, and pyocyaneus emulsion into the femoral artery of rabbits and the same dose into the muscle. He used calomel, from 0.1 to 0.5 gram (1.543 to 7.716 grains) in 10 c.c. (2.71 fluidrams) of water; turpentine 0.5 to 1.5 gram (7.716 to 23.146 grains) in 10 c.c. of water in emulsion; pyocyaneus 1.0 to 3.0 c.c. (16 to 48.6 minims) of thin emulsion. The muscles were examined at varying periods after the treatment—three, seven and twenty-four hours. Saltykow found that the gross appearance of the muscles varied with the amount of the agent used. The muscle might be pale, or look much like the spleen, depending upon the amount of the agent employed. Within a few hours the muscle became stiff and inelastic. There was proliferation of the muscle-nuclei, as found in muscle changes of all kinds, in atrophy after section of the nerve supply, and in all other changes of pathologic origin. The disappearance of contractile substance was noted, and the presence of empty sarcolemma sheaths, infiltration of large and small lymphocytes, hyaline, granular and vacuolar degeneration of fibers. There were red areas from hemorrhage and white areas from cellular infiltration. In other words, there was nothing characteristic in the muscle changes to betray the etiology. It is only the severity of the process and the chronicity which determine the muscle changes in most of the processes. We find no explanation for the etiology of the disease in most of the cases of acute myositis.

A review of the reported cases of myositis associated with rheumatism shows very essential differences in the gross lesions in the course of the infection, and in the end-results. The rheumatic cases are not accompanied by acute or chronic skin manifestations like those found in dermatomyositis, and the rheumatic cases are not accompanied by perimyositis. The rheumatic cases of myositis which the writer has seen showed only intramuscular lesions, which involved single muscles and groups of muscles. The first case described is a very good instance of how extensive rheumatic myositis may be, and still confine itself within the sheath of a muscle. In this case there was an inflammation of the entire adductor magnus, and, in spite of its large extent, the single large muscle could be very clearly differentiated from all of its neighboring muscles. The rheumatic cases strongly suggest intramuscular metastatic infections, whereas dermatomyositis gives the symptoms of perimyositis with subsequent invasion of the intramuscular structures. A nervous factor has been introduced into the nomenclature with dermatomyositis on inadequate evidence. Peripheral nerve lesions were found in affected areas, but this involvement of the peripheral nerve was secondary to local inflammation and did not share in the etiology of the disease.

Treatment.—There is no treatment of dermatomyositis which is of value in either the acute or the chronic stage. Until some further progress is made in our knowledge of the infection and immunity to the disease, we cannot reasonably expect successful specific therapy in the acute or chronic stages of dermatomyositis. **Baths** and **fomentations**, and **massage** will no doubt ameliorate the symptoms and probably modify the stiffness which is so annoying to the patient. **Thiosinamin** might be used in the chronic stage, but the author has observed no success attending its employment. There is **little** to be expected from **salicylates**, which are so effective when used in sufficient doses for the treatment of acute multiple arthritis. In the author's own experience the salicylates have had no effect upon the duration or severity of the muscular lesions. We cannot look upon this therapeutic failure as evidence against the theory that myositis has etiological factors in common with synovitis. Although salicylates are very effective in acute rheumatic synovitis, they fail to affect endocarditis, endophlebitis, inflammations of the serous membrane, and chorea, all of which frequently occur coïncidently with acute rheumatic arthritis; and it is quite usual to see the joint lesions promptly subside under the influence of salicylates, while the above-mentioned lesions remain refractory to this treatment.

PATHOLOGY.—The pathology of dermatomyositis is in a very vague state. There are pathological indications that a certain group within this disease composes a clinical entity with a common etiology. Whether the chronic cases such as the author described have the same etiology as the earlier cases reported by Unverricht, Wagner, and Hepp, is doubtful, although there is much uniformity in the sequence of events, in the skin and muscles in both the acute and fatal cases and the chronic cases which survive. That the disease is infectious seems very certain. Sick[3] reported 4 instances occurring in the case of nurses in the psychiatric clinic at Tübingen. There is very little in Sick's article which is illuminating, so far as the character of the disease is concerned, but the article is important inasmuch as it shows that an epidemic of multiple myositis may occur. There is further evidence that dermatomyositis is caused by an organism which has a selective property for skeletal muscles. Martinotti[4] describes the case of an old man who developed fever and sepsis, and died within a few days. An autopsy showed several abscesses, the size of millet seeds, in the kidneys. The organism was isolated, and when cultures of either 1 c.c. or 1/10 c.c. were injected into animals, the colonization was always found in the muscles of the abdomen, hind- and fore-legs. Abscesses were found in the muscles, but they were always small—the size of a millet seed; Martinotti calls the organism *Staphylococcus pyogenes aureus myositidis.* He reported the autopsies only to illustrate the selective property of this organism for the muscles.

Mayesima[5] observed a case of polymyositis from which he recovered *Micrococcus albus liquefaciens.* He proved agglutination of the organism with the serum of the patient. Mayesima believed that this patient was infected through the tonsils, and calls attention to the fact that the disease is never associated with suppuration of the muscles.

Schmitz[6] cultivated *Staphylococcus pyogenes aureus* from a patient with acute multiple myositis, and was able to reproduce myositis in guinea pigs. The heart, liver, lungs and spleen were normal in experimental animals, and Schmitz thinks that the organism has a preference for skeletal muscles. He endorses the work of Martinotti, and states that in his animals there were abscesses in the muscles, but that the abscesses were extremely small.

Herbert Fox's[7] case was one of polymyositis from which he recovered a *Micrococcus pyogenes*. There were some cultural differences between this organism and *aureus* and *albus*. Fox suggests that the organism may be *Micrococcus pyogenes myositidis*. He found that in the fifth generation the organism was agglutinated by the patient's serum.

Gout.—The objective signs of intramuscular changes in gout are not as clearly defined as are the gross pathological lesions of the rheumatic myositis. Inflammations of tendon-sheaths, bursæ, fascia, and aponeuroses are not uncommon in gout. Subcutaneous nodules occur in gout, and are just as well-defined and painful as are those which are more commonly seen, viz., the rheumatic nodules. An instance of this was seen in the case of an elderly woman suffering from gout and diabetes. She complained bitterly of pain in the hands, which rendered them almost useless. The fingers could not be extended, nor could the hands be firmly closed on account of the severe pain. The hands were both held in a semifixed position on account of the pain which attended both flexion and extension of the fingers. Over the ends of the third metacarpal bone of each hand, between the skin and palmar fascia, a small nodule the size of a French pea could be palpated, which had a firm consistency and was slightly mobile on its fascia attachment. These nodules were exquisitely sensitive to pressure. Under a dietetic regimen (which followed the starvation treatment), with the use of **atophan,** the pain and the nodules subsided. That fascia and tendons may be the seat of gouty deposits has long been known, but there are no clear accounts of gouty deposits within the skeletal muscles. However, gouty patients suffer from muscular cramps and muscular pains which are attended by the appearance of sensitive pressure points, and the muscles are sensitive to stretching, quite like the muscles in rheumatic myositis. Inferentially, there seems excellent ground for suspecting the occurrence of intramuscular gout. This form of myositis is more amenable to treatment than is the rheumatic form. Patients with gouty manifestations in the bursæ, tendons and fascia respond quite well to treatment. The gouty **dietetic regimen** should be adopted, and **atophan** (tablets), grains 7½ (0.492 gram), q.i.d., in half a glass of water after food, is very helpful. The atophan is best employed by using it three or four consecutive days in a week and then intermitting its use for the remainder of the week.

Myositis Fibrosa.—This very unusual disease is described by Batten.[8] It begins as a subacute inflammation of the muscles, and produces a chronic myositis, which seeks successively various groups of muscles and slowly advances. The lower extremities are usually attacked first, but cases are reported in which the inflammation started in the sternomastoid muscles and spread to the neck and back and intercostals, and later to the abdominal muscles. The case described by Batten was that of a child six years old. The disease began in the latter part of the first year of life. The condition progressed slowly. The child did not seem to have any pain, in which respect this case differed from other reported cases. Owing to the extremely hard and contracted abdominal muscles, the spine was fixed in a curved position and could not be straightened. The arms were fixed so that they could not be extended or adducted. He was rigidly fixed, and, in the flexed position, was unable to move or be moved except as a whole.

The writer has seen only one instance of myositis which could be termed myositis fibrosa. This patient was seen during a visit to the City Hospital in Cleveland. The patient was a young woman, twenty-five years old, who had suffered from her disease for nearly two years. She was greatly emaciated, and the ileofemoral and thigh muscles and the muscles of the shoulder-girdle were all involved, and, as in the case described by Batten, there was marked retraction of the recti abdominis. The muscles were very small, indurated, and sensitive to pressure. Any attempt to stretch them caused violent pain. The skeletal muscles were all transformed into small indurated bands. No joints were involved, and no other lesion in the body could be demonstrated beyond the extensive involvement of the muscles. The patient died shortly after admission to the hospital, and unfortunately autopsy was forbidden.

The etiological factor in this case remains unexplained, and so does its pathology. It was not even possible to offer any contribution to the gross pathology of the disease, but it seems worth while to mention the case because the disease strikingly conformed to the distribution and end-results of other cases of myositis fibrosa. The history and development of symptoms in this patient clearly indicated myositis, and the disease remained uncomplicated myositis up to the time of death.

Syphilitic Myositis.—Syphilitic myositis is a comparatively rare complaint, but it seems very probable that a syphilitic inflammatory process in the muscle may frequently occur without producing any symptoms of either a subjective or an objective character. A large proportion of the reported cases have shown the location to be in the ends of the muscle, near its junction with a tendon or aponeurosis. We may have a gummatous form, with necrosis and subsequent invasion of the skin, so that the disease will simulate a caseous tuberculous gland. The writer saw one such patient who had several sinuses about the lower end of the sternomastoid muscle. The lesion proved to be an ulcerating gumma from the lower end of the muscle, and promptly healed after antisyphilitic treatment. The sternocleidomastoid muscle, biceps, trapezius, masseter and temporal muscles have all been mentioned as favorite locations for syphilitic myositis. The locations have varied in the experiences of different writers, but the author's own experiences have been confined to the sternocleidomastoid, the biceps, and the rectus abdominis. The rectus abdominis case was in a woman about thirty years of age, who discovered primary swellings in the upper extremity of the right rectus muscle. The mass was not sensitive to pressure, nor was it sensitive to activation of the muscle or to stretching. The entire mass promptly disappeared under antisyphilitic treatment, returned about a year later, and again disappeared under the same therapy.

Trichinosis.—In one instance of acute trichinosis, the patient, a young woman, entered the hospital with severe pain in the muscles of the upper and lower extremities. The patient was compelled to lie at rest in bed on account of the pain and the loss of muscular power. The muscles were sensitive to pressure and exquisitely so to stretching, but activation of the muscles was not painful. The patient could hold her leg extended on the thigh against strong resistance and suffer no pain, but if the knee was bent she complained of severe pain in the quadriceps muscle. The only diagnosis which could be made from the objective examination and the history was that of an acute multiple myositis. The blood-count showed no increase of eosinophils, but an excised fragment of the quadriceps muscle revealed an abundance of larvæ. This instance of trichinosis is mentioned because one may encounter instances where neither the history nor the clinical picture indicates anything beyond acute myositis. A widely-distributed acute myositis should always arouse a suspicion of trichinæ.

Gonorrheal Myositis.—This is a very rare complication of gonorrhea. The writer had one patient who developed a very painful suppuration of the lower extremity of one of the peroneal muscles of the right side. The abscess was opened and gonococci were recovered from the pus.

No doubt of all the causes of acute muscular diseases, exposure to moisture and cold, gout, and rheumatism are the most frequent. Other infectious sources are rarely seen, but although they are rare, one must not neglect consideration of a muscle as the metastatic seat of any variety of infection.

Muscular Atrophy and Joint Diseases.—A never-failing but perplexing accompaniment of joint disease is an atrophy of the muscles on the proximal side of the joint. In the case of the knee-joint, the quadriceps muscle is invariably atrophied. When the hip-joint is involved, the gluteus maximus is atrophied. When the shoulder-joint is diseased, the deltoid muscle is always atrophied; other muscles may be involved, such as the supraspinatus and infraspinatus, and should the synarthrosis between the acromion process and the clavicle be involved, it is common for the cervical portions of the trapezius to be involved. The muscles of the arm are usually involved in diseases of the elbow, and atrophy of the forearm attends inflammation of the wrist-joint. When the carpal and phalangeal joints are involved, we see very marked atrophy of the interosseous thenar and hypothenar eminences. Deformity following multiple arthritis may be due far more to muscular atrophy than to structural changes in the joint itself, and the protracted recovery of function after an attack of arthritis is largely due to muscular atrophy. Occasionally in multiple arthritis which has not lasted long and has left no deformity of the joint itself, the muscular atrophy may be so severe as to simulate primary muscular atrophy. Muscular atrophy is distinctly an attendant upon synovitis and does not result from peri-articular lesions. Patients may have peri-articular deposits about the knee-joint which occasion a great deal of disability and much pain, but if the synovial sac is not involved, there will be no atrophy of the quadriceps muscle; whereas a very moderate synovitis of the knee-joint, which may last only a few days, will cause a clearly demonstrable atrophy of this large muscle. The atrophy is not due to disuse, for the disuse may be quite as pronounced from any other source, but the promptness and the degree of atrophy are strikingly characteristic of all cases in which there is a lesion of the synovial sac. The tendon reflex of the muscles is always exalted; in fact, atrophy with exaggeration in tendon reflex is such a constant accompaniment of synovitis of any joint that, if the patient gives a history of recent inflammation of the knee-joint and there is no atrophy or exaggeration of the patellar reflex on the affected side, one is justified in assuming that there could have been no recent lesion of the knee-joint.

The pathological physiology of both the atrophy and the exaggeration of the reflexes is unexplained, and the author knows of only one point of view which throws any light upon the subject. Hoffa of Würzburg conceived the idea years ago that the atrophy was due to some afferent impulse along the nerve supply of the affected region. His first procedure was to cut all of the posterior nerve-roots of the sciatic nerve. He then injected bacterial cultures into the knee-joint in animals whose nerve supply was intact and also into the animals in which there had been a previous section of the posterior nerve-roots. Hoffa found that, when the posterior nerve-roots to the region were cut, the acute infectious synovitis was not attended by muscular atrophy; whereas it invariably occurred when synovitis was produced in animals with intact nerve supply. This, of course, does not amount to a solution of the problem, but it does offer considerable evidence that the atrophy and exaggeration of reflexes are due to some unknown modification of the lower neuron through the agency of the afferent paths of the peripheral nerve.

REFERENCES

1. Eulenburg. Realencyklopädie des Gesammtheitskunde, 4th Ed., 1887, xii, 1.
2. Saltykow. In Virchow's Archiv, 1903, clxxi, 118.
3. Sick. Münch. med. Wchnschr., 1905, lii, 1092.
4. Martinotti. Centralbl. f. Bakt. u. Parasitenk., 1898, 1ste Abt., xxiii, 877.
5. Mayesima. Deutsch. Ztschr. f. Chir., 1910, civ, 321.

6. Schmitz. Centralbl. f. Bakt. u. Parasitenk., Original, 1912, 1ste Abt., lxv, 259.
7. Fox, H. Am. Jour. Med. Sci., 1913, clxv, 879.
8. Batten. Tr. Clin. Soc., London, 1904, xxxvii, 12-40a.

SECTION VIII

DISEASES OF THE KIDNEY

CHAPTER I

DISEASES OF THE KIDNEY

By J. B. McElroy, B.S., M.D.

Congenital nephropathies, p. 550:—Ectopic kidney, p. 550—Congenital malformations, p. 551:—Congenital single kidney, p. 551; Congenital atrophic kidney, p. 553; Lobulated fetal kidney, p. 554; Fused kidneys, p. 554:—Horseshoe kidney, p. 554; Fused single kidney, p. 556—Variations in renal pelvis and ureters, p. 557.

Movable kidney, p. 558:—Etiology, p. 559; Symptomatology, p. 559; Diagnosis, p. 563; Treatment, p. 565; Pathology, p. 566; Historical summary, p. 566.

Uremia, p. 566; Definition, p. 566; Symptomatology, p. 566; Clinical varieties, p. 570; Treatment, p. 571:—Eclamptic equivalents, p. 572; Uremia with kidney insufficiency, p. 573.

Nephropathies of circulatory origin, p. 575:—Chronic passive congestion of kidneys, p. 575:—Definition, p. 575; Etiology, p. 576; Symptomatology, p. 576; Treatment, p. 581; Pathology, p. 583.

Focal atherosclerotic kidney, p. 584:—Symptomatology, p. 584; Treatment, p. 585; Pathology, p. 585.

Nephropathies generally included under the genetic term Bright's disease, p. 585:—Introduction, p. 585—Nephrosis, p. 588:—Definition, p. 588; Etiology, p. 588; Symptomatology, p. 590; Diagnosis, p. 594; Complications, p. 594; Clinical varieties, p. 594; Treatment, p. 595; Prognosis, p. 597; Pathology, p. 597.

Amyloid kidney, p. 599.

Necrotizing nephrosis, p. 601:—Symptomatology, p. 601; Treatment, p. 603; Prognosis, p. 603; Pathology, 604.

Glomerulonephritides, p. 604:—Etiology, p. 604—Diffuse glomerulonephritis, p. 608:—Acute diffuse glomerulonephritis, p. 609:—Symptomatology, p. 609; Complications and sequelæ, p. 613; Treatment, p. 613; Prognosis, p. 618; Pathology, p. 618—Chronic diffuse glomerulonephritis, p. 627:—Etiology, p. 627; Symptomatology, p. 627; Diagnosis, p. 629; Complications, sequelæ and associated conditions, p. 630; Treatment, p. 630; Pathology, p. 630:—End stage of chronic diffuse glomerulonephritis, p. 637:—Symptomatology, p. 637; Diagnostic features, p. 642; Treatment, p. 643; Prognosis, p. 644; Pathology, p. 645.

Focal nephritides, p. 654:—Acute focal glomerulonephritis, p. 654:—Pathology, p. 655—Chronic focal glomerulonephritis, p. 656—Septic interstitial nephritis, p. 656:—Pathology, p. 656—Embolic focal nephritis, p. 656:—Pathology, p. 657.

The scleroses, p. 657:—Introduction, p. 657—Benign hypertension, p. 658:—Etiology, p. 658; Symptomatology, p. 660; Diagnostic features, p. 665; Treatment, p. 666; Prognosis, p. 668; Pathology, 669—Malig-

nant hypertension, p. 676:—Etiology, p. 676; Symptomatology, p. 677; Diagnostic features, p. 680; Treatment, p. 680; Prognosis, p. 680; Pathology, p. 680.
Bibliography, p. 686.

CONGENITAL NEPHROPATHIES

Congenital nephropathies may be considered under the head of displacements and malformations. Congenitally displaced kidneys are fixed and may or may not be deformed. Displacements with malformations will receive attention with the malformations. Of the congenital displacements of the kidneys, the most important is the ectopic kidney.

Ectopic Kidney.—Synonyms are pelvic kidney and dystopic kidney. The ectopic kidney is fixed in the bony pelvis or at the sacral promontory across the spine, and receives its blood supply from adjoining blood-vessels, such as the iliacs.

Braasch found 3 cases of ectopic kidney among 36 anomalous kidneys. Kelly and Burnam have had 8 cases. The right kidney is more frequently fixed in abnormal position than the left. The condition is due to the arrest of the kidney in its ascent during fetal development. If this takes place during the period from the second to the fifth week, it will be fixed in the pelvis; if later, it will be found above.

There may be no symptoms present, or symptoms due to pressure of the displaced kidney may be complained of, such as pains referred to the back and lower abdomen and intestinal disturbances. Symptoms due to associated pathological lesions such as hydronephrosis and calculus may also be present. On palpation a tumor, which may be mistaken for diseased uterus or adnexa or for an appendiceal mass, will be detected.

Cystoscopic examination may show an anomalous ureteral opening. The ureteral catheter can be passed only a short distance, but if it has passed into the pelvis of the kidney, as indicated by the discharge of urine, the abnormal position of the kidney may be located. This will be accomplished better by pyelography which will also show any anomalies of the renopelvic outline which may be present.

The diagnosis of etopic kidney is of importance to the surgeon and obstetrician as it is likely to be confused with certain surgical conditions and sometimes causes serious dystocia.

The detection of a retroperitoneal mass associated with large blood-vessels, by rectal or vaginal examination, might suggest the presence of an ectopic kidney if one kept this condition in mind as a diagnostic possibility. Its presence can be confirmed only by special examinations —ureteral catheterization and pyelography.

According to Braasch, the most frequent complication of ectopic kidney is hydronephrosis. Kelly and Burnam found calculus in one. Genital anomalies are frequently associated with pelvic kidney.

The kidney is usually in the pelvis or lying across the spine at the sacral promontory, though it has been found in other peculiar positions, as near the inguinal ring and in a congenital umbilical hernia. The pelvis of the kidney lies in front and the kidney itself is flattened posteriorly with deep anterior grooves to fit its bed. The vessels are abnormal, usually arising from those nearest to it as the common iliac, external iliac, etc.

Congenital Malformations.—Congenital malformations of the kidney have to do with variations in the number, size and form of the kidneys, and with variations in the pelvis, ureters and renal blood-vessels. Congenital absence of both kidneys has been noted in monstrosities, but the condition is incompatible with postnatal life. True supernumerary kidneys require that more than two anlagen be present and that they remain separate throughout development and ascent. True supernumerary kidney is very rare and has no clinical importance.

Variations in form and size have to do with lobulated fetal kidneys, fused kidneys and congenital cystic kidneys. The latter will be considered under a separate heading.

CONGENITAL SINGLE KIDNEY.—Synonyms are solitary kidney, and asymmetrical kidney. This condition requires that there be a complete absence of the kidney on one side.

Anders in a careful review of the literature up to 1910 determined that the expectation of the congenital single kidney gives a ratio of 1 in 1817 autopsies and that there was a total number of 286 cases. Of Kuster's cases 10 per cent. were in new-born babies. Of 154 cases collected by Anders, 34 were under ten years of age, which includes 13 premature births; 62 were between ten and fifty years of age; and 50 were over fifty years of age. Of 248 cases collected by Anders, 159 were males and 89 were females.

Agenesis takes place early in fetal development from the third to fourth week. The anlage fails to develop from the wolffian duct which may itself be insufficiently developed; or the anlage may pass through the first stage, but becomes arrested or absorbed before it has completed its ascent.

The subjective symptoms are of little value, and when present are due to associated pathological lesions. On palpation the remaining kidney may be found enlarged. This will, however, only be suggestive since one of two kidneys may be found enlarged and lying low, and a tumor of surrounding organs may simulate an enlarged kidney. Cystoscopy will usually reveal only one ureteral orifice. Caution must be exercised in deciding upon the absence of one ureteral orifice, especially in an inflamed, contracted bladder. The injection of indigocarmin will here be of great assistance. If only one ureteral orifice is present, close inspection may reveal hypertrophy of the muscular ring about the ureteral orifice and the urine escaping more frequently and in greater volume than normally. Several cases have shown the presence of a portion of the ureter of the absent kidney. Under this condition two ureteral orifices will be present. The ureteral catheter can be passed only a short distance, and no urine will be seen coming from this side. Pyelography will show the pelvis of the kidney enlarged and normal in outline.

The diagnosis of congenital single kidney is of extreme importance to the surgeon, for in contemplated operations on this organ it is necessary to know whether both kidneys are present. Ransahoff has collected the records of eleven operations on solitary kidneys; of these four were nephrotomies and seven nephrectomies. The nephrectomies were fatal in from one to eleven days. The condition is perhaps of no less importance to the internist in view of the alarming symptoms which develop in case the remaining kidney becomes diseased, which is a result not unusual. The diagnosis must be made by special examination—cystoscopy, ureteral catheterization and pyelography, the results of which have been described above. Sometimes one kidney has been destroyed by pathological processes and it will be necessary to differentiate between this condition and congenital single kidney. In the acquired single kidney the signs of inflammation around the ureteral orifice are present, the ureteral orifices are usually in normal position, and as a rule the pelvis is not enlarged (Braasch). Functional kidney tests may be of corroborative value in the diagnosis of congenital single kidney, as the output of phenolsulphonephthalein from the compensatorily hypertrophied kidney may approximate the normal.

Complications are frequent in the congenital single kidney. Of 170 cases collected in 1910 by Anders, 79 showed morbid changes other than compensatory hypertrophy. These were as follows: chronic interstitial nephritis, 19; chronic nephritis (variety not specified), 11; chronic parenchymatous nephritis, 2; ureteral calculi, 9; pelvic calculi, 6; hydronephrosis, 4; pyelonephritis, 10; cystic kidney, 3; tuberculosis, 2; "diseased" kidney, 3; stone in the bladder, 1; carcinoma of the kidney, 1; cloudy swelling, 1; congested kidney, 1; amyloid kidney, 1; fatty kidney, 1; abscess of the kidney, 1. Of Braasch's (1912) 6 cases, there was tuberculosis in one and a kinked ureter producing partial obstruction in one. Of 3 cases of Kelly and Burnam (1914), there was stone and tuberculosis in one, stone and hydronephrosis in one, and tuberculosis in one.

Congenital single kidney is frequently associated with genital hypoplasia and sometimes with the absence of the adrenal gland on the affected side. Of 255 cases collected by Radasch (1908), 100 showed defective genitals. In 90 of these the lesion is specified. Forty-nine were in males as follows: absence of vas deferens, 22; absence of seminal vesicles, 20; absence of ejaculatory ducts, 9; absence of testicles, 15. Forty-one were in females as follows: uterus entirely absent or bicornate, 12; vagina absent or reduced by one-half, 5; oviducts absent, 9; ovaries absent, 4. In 151 cases collected by Anders, the suprarenal gland was absent on the affected side in 27.8 per cent.

There is always compensatory hypertrophy in the congenital single kidney. It is claimed that this is due to hyperplasia of the glomeruli and tubules brought about during fetal development, rather than to enlargement of individual glomeruli and tubules. During the ascent the kidney may cross the middle line and lodge in the lumbar region of the opposite side. There is usually an abnormal number of blood-vessels—3 to 5 arteries and 3 to 4 veins arising from the large abdominal trunks. An unusual number of vascular twigs supplying fat or connective tissue are said to indicate the presence of a rudimentary kidney; and a number of large obliterated vessels are likewise said to indicate that the kidney had existed and had been destroyed by a pathological process. Of 153 cases in which the kidney and ureter were absent, L. Polack, in 1905, found that 89 were on the left side, 56 were on the right side and on the side not mentioned in 8. Of 286 collected by Anders in 1910, 153 were on the left side, 120 on the right, and on the side not stated in 13.

Congenital Atrophic Kidney.—Synonyms are rudimentary kidney, fetal kidney, infantile kidney, and renal hypogenesis. There are two groups of these kidneys: in one there is development from only a portion of the renal anlage; in the other the kidney shows the usual form and construction, but is greatly reduced in size.

Morris places the frequency of the congenital atrophic kidney as .02 per cent. of all autopsies; Braasch saw 6 cases in 36 anomalies and Polack found 16 cases in 264 anomalies. The age at which death occurs varies. Of 66 cases collected by Gastaldi, 32 were in males, 10 were in females, 18 not stated. Of 9 cases of Coplin, 5 were in males and 4 were in females. Arrest in the embryonic development occurs from the seventh to the ninth week. Coplin emphasizes the relation of the condition to defective arteriogenesis.

There may be no symptoms at all, but several observers have attempted to construct a clinical syndrome characteristic of so-called hypogenetic nephritis. Besancon calls attention to chlorosis, headache, vomiting, lassitude, slight puffiness of the eyelids, slight diffuse edema of the lower extremities, frequent micturition and pale abundant urine. In a case studied by Stengel there was pregnancy associated with toxemia and eclampsia. The patient gave a history of kidney trouble all her life; the systolic blood-pressure was constantly above 200 mm.; there was a trace of albumin and a low specific gravity. The phthalein excretion was 40 per cent. in two hours and the non-protein nitrogen of the blood was from 33 to 36 mgs. (.5082 to .5564 grains) per 100 c.c. (3.38 fluid ounces).

With slight atrophy cystoscopic examination will show nothing abnormal. With marked atrophy it may show atrophy of the circular muscle about the meatus, slight meatal contraction and only an occasional and slight discharge of urine. The other meatus will show a compensatory increase. Due to the atrophy of the ureter which is usually present, it will be difficult to pass even a small catheter. Pyelography may show the pelvis so rudimentary as to corroborate the above findings.

In the diagnosis, nephritis, toxemia or uremia and especially cardiorenal disease in a young person are suggestive. The diagnosis can, however, be established only by the results of the special examinations mentioned above. Quantitative functional differences of both kidneys may be of corroborative value. Under certain pathological conditions atrophy of one kidney may be acquired. This may often be excluded by the presence of genital hypoplasia which frequently accompanies the congenital atrophy.

The associated genital anomalies are usually on the same side as the renal defect, but Lombroso has reported a case in which it was on the opposite side. Renal dystopia and displacement of ovaries and testes may be present.

In those cases in which a portion of the renal anlage fails to develop, the pelvis and ureter may be represented by only a formless pouch at the end of a tube or a solid cord; or the cortex may develop but not to the extent of producing lobulation and subdivision of the medullary substance, when one or two pyramids instead of the usual number will be present. The anomaly is usually confined to one kidney, the other showing compensatory hypertrophy. The weight of the affected kidney may vary from one gram (15.43 grains) to normal. In 5 of Coplin's cases, the smaller averaged 75.8 grams (1169.594 grains) in weight and the larger 140.4 grams (2165.372 grains). Macroscopically, the arteries are smaller than normal and have a small lumen in proportion to the thickness of their walls. Microscopically, evidence of arterial hypoplasia is seen in fragments of the external elastic membranes in the perivascular tissue, in its uneven thickness and diffuse waviness, and in the abnormal thickness of the muscular coat which contains more fibrous than muscular tissue. Further it is seen in the long irregular sweeps of this internal elastic membrane, and in its irregularity, imperfection and fragmentation. Superimposed upon these signs of defective arteriogenesis are the lesions of arteriosclerosis and primary contracted kidney. Of 60 cases analyzed by Coplin, 32 involved the right kidney and 28 the left.

THE LOBULATED FETAL KIDNEY.—Lobulation of the kidney usually disappears after the fourth year of life. Its persistence longer indicates that the growth of the cortex has not been vigorous enough to obliterate the depressions, or that the cortical columns were of such depth that the usual postfetal cortical growth was insufficient to fill in the grooves.

Most lobulated kidneys have abnormal arterial circulation, while the veins are more apt to be regular. They are much more susceptible to disease than smooth kidneys, tuberculosis being relatively frequent.

FUSED KIDNEYS.—There are two varieties of fused kidneys, the horseshoe kidney and the fused single kidney of which there are several subvarieties.

The Horseshoe Kidney.—Synonyms are ren arcuatus, and ren unguliformis. While, as the name indicates, this kidney in shape resembles a horseshoe, some of them are irregular and resemble the letter L. They result from fusion of the embyronic anlagen before the ascent of the kidneys from the pelvis take place.

The combined statistics of Morris and Socin show that horseshoe kidney occurred in .02 per cent. of 1600 autopsies. Braasch saw 8 cases in 36 anomalies of the kidney. It is more frequent in women than in men. Fusion of the embyronic anlagen takes place before the ascent of the kidneys out of the pelvis, that is, before the seventh week.

There may be no symptoms at all. Rosving has described a rather characteristic clinical syndrome occurring without the presence of pathological lesions. There is pain referred to the abdomen, lumbar region and epigastrium; it radiates downward; it is aggravated by standing, continuous jarring and muscular exercise; it is mitigated by rest and relieved by prolonged rest. There is also throbbing and a sense of pressure in the abdomen, aggravated by bending forward. Symptoms due to associated pathological lesions are present. With hydronephrosis there is swelling in the region of the displaced kidney, limitation or retention of urine, sudden relief of pain with the passage of a large quantity of urine of a low specific gravity, and chronic dragging pains referred to the back and lower abdomen. With pyonephrosis there is steadily increasing pain, increased by pressure over the swelling, relieved by discharge of pus, and associated with febrile symptoms. With nephrolithiasis, there is pain, associated with hematuria and often pyuria, increased by manipulation and exercise, and relieved by rest. With tuberculosis, there is enlargement with tenderness in the lower abdomen; slight hematuria, pyuria and the presence of tubercle bacilli in the urine; pollakiuria and dysuria with irritation of the ureteral orifice and the escape of purulent urine on the affected side; and a febrile temperature and evidence of tuberculosis elsewhere.

With cystic tumors there will be a swelling in the lower part of the abdomen. The swelling does not fluctuate; it is rounded and nodulated on the surface, and its general contour may suggest the horseshoe shape; it is not painful on pressure.

The horseshoe kidney may be associated with thrombrosis of the iliac and femoral veins giving rise to edema of the legs and ascites. Upon palpation under an anesthetic, a mass might be felt and its contour made out in a thin individual as in a case of Newman. There was fusion of the upper pole of the kidney with the convexity upward.

The radiographic shadow is usually too inexact for satisfactory interpretation, though it is occasionally suggestive, especially when there is the shadow of a stone in the lower median abdomen. Meatoscopy may be of corroborative value. Obstruction of the ureteral catheters at a low level may suggest a renal anomaly. Pyelography will accurately determine the position of the pelvis as well as any deformity of the pelvis or ureters which may be present.

The diagnosis will be suggested by the clinical syndrome, by palpation, and the presence of genital defects which are frequently present. and definitely determined by the results of the special examinations, particularly pyelography.

Cryptorchidism, hypospadias, atresia of the veins, double or bicornate uterus, absence of the vagina and other genital defects have been found associated with horseshoe kidney. According to C. H. Mayo, the most frequent complication is hydronephrosis, which is more likely to occur in moderately young individuals. Pyonephrosis and lithiasis are seen less frequently and usually occur in middle age and later. Tuberculosis, sarcoma, and cystic tumors are also occasional complications.

In 90 per cent. of the cases fusion takes place at the lower poles of the kidney because they are closer together in the early stage of development. At the seventh week of fetal development, before which time the fusion usually takes place, the kidneys have not rotated; therefore the pelvis is usually found in front of the organ. The pelves do not fuse, because they are developed before parenchymatous fusion occurs. The ureters are frequently divided. The vessels are more numerous than usual, arise from the nearest arterial source and usually at a lower lever than normal. They branch and enter the parenchyma mostly behind the pelvis. The kidneys as a rule do not rise higher than the level of the aortic bifurcation. The connecting bridge may be composed of only a fibrous band of tissue or more frequently of cortical tissue without medulla. The bridge is on a level with the aortic bifurcation, its anterior surface is lobulated with distinct depression in the center and its posterior surface is smooth. In about 10 per cent. of the cases fusion takes place at the upper poles of the kidney.

The Fused Single Kidney.—There are several varieties of this malformation, the unilateral elongated kidney (ren elongatus), the scutiform or shield-shaped kidney (ren scutaneous), and the lump kidney (ren informis). The symptoms are much like those of the congenital single kidney. Physical examination reveals a tumor which may simulate tumor or disease of the pelvic organs, such as ovarian or uterine tumors, hydrosalpinx, pyosalpinx, an appendiceal mass, tumors of intestinal, pancreatic or mesenteric origin, or bony tumors of the pelvis. Cystoscopy is usually of not much value as two normal ureteral orifices will be found in the normal position. Upon ureteral catheterization and injection of the pelvis, the condition will be suggested by the pain being referred to only one side. The renal pelvis may be accurately located by metal catheters or better by the injection of thorium and radiography.

Stein has called attention to the particular importance of the diagnosis to the surgeon to prevent catastrophies and unnecessary lumbar incisions and to the obstetrician, as this malformation may form even more serious obstacles in parturition than the pelvic kidney.

The presence of the tumor makes it necessary to differentiate the fused single kidney from cancer of the colon, hepatosis, nephroptosis and from a pathologically hypertrophied kidney and from a congenital single kidney. In cancer of the colon, the kidney mass is smooth and regular; there is no tympany above and below the kidney mass; cancer of the colon is usually associated with hemorrhage and intestinal obstruction; if there is no functional evidence of the latter, it may be determined by injection of bismuth and radiography. In hepatosis and nephroptosis, the liver and spleen are movable and can be raised to some degree; the fused single kidney is fixed in abnormal position. The pathologically hypertrophied kidney and the congenital single kidney can be differentiated and the diagnosis in all cases can be found only by special examination, especially pyelography.

Of 55 cases collected from the literature by Stein, the following complications were shown: tuberculosis, 3; nephritis, 2; hydronephrosis, 1; hydronephrosis and nephrolithiasis, 1; pyonephrosis, 1; suppurative pyelonephritis, 1; nephrolithiasis, 1; hypertrophy of one kidney and atrophy of the other, 1.

Associated genital malformations are not so frequent as in pelvic kidney, but they occasionally occur. In the unilateral elongated kidney, both renal anlagen fuse and ascend together into one lumbar pocket. There are two varieties of the unilateral elongated kidney. They follow:

(1) The simple elongated kidney (ren elongatus simplex). In this variety, one kidney is on top of the other, the hilum is turned toward the vertebral column, the arteries arise separately from the aorta, the ureters and pelves are separate, and represent the persistence of the six weeks' stage of embryonic development.

(2) The sigmoid kidney (ren sigmoidus). In this variety, one kidney is above with the hilum in the usual position; the other is below with the hilum facing in an opposite direction; there is a groove where the kidneys fuse; the ureters may cross; the arteries are separate, abnormal in origin and there is sometimes an accessory artery. In the scutiform or shield-shaped kidney, fusion takes place early—four to six weeks—and is complete; the position is low in the median line of the body, usually in the hollow of the sacrum; there are usually two arteries, rarely one; there are two varieties, the round and the flat.

The lump kidney (ren informis) is an irregular shaped mass composed of lobes of different sizes. Its position is just above the sacral promontory. There are from one to four short ureters in the anterior surface. The vessels enter the parenchyma in the depressions between the lobules in various positions.

The fused single kidneys occur about one time in 8,178 autopsies. Stein in 1916 collected 57 cases from the literature. It is about twice as frequent in men as in women, which is in contrast with reference to the occurrence of horseshoe kidney in the two sexes.

VARIATIONS IN RENAL PELVIS AND URETERS.—Of the variations in the renal pelves and ureters may be mentioned variations in the form and position of the pelves, duplication of the pelvis, cleft ureters, double and triple ureters, and anomalies of the lower end of the ureters.

Anomalies of the upper end such as obliquity of insertion of ureter into pelvis, absence of pelvis, and half a pelvis may give rise to symptoms of hydronephrosis. Abnormal openings of the lower end of the ureter in the male may also give rise to symptoms of ureteral dilatation and hydronephrosis. Incontinence and constant dribbling of urine which is a frequent and very annoying symptom in the female is not present in the male, since the abnormal opening is never anterior to the compressor urethræ in the male.

The diagnosis is established by cystoscopy, ureteral catheterization by metal catheters, and pyelography. Precocious splitting of the ureter, cleft ureter, is due to the nondevelopment of the primitive renal pelvis, the pole tubules developing precociously and then ascending parallel to each other. The cleavage may extend downward into the undivided portion of the ureter so that finally the latter is cleft right to its entrance into the bladder. Double and triple ureters are of a regressive nature. They arise as two or three ureteric buds from the primitive excretory ducts. These multiple ureteric buds do not develop equally, the most caudal one showing the strongest development, not only as regards the expansion of its ureteric tree, but also as regards the height that it reaches in development (Felix). The ureter will open into the rectum if the wolffian duct and ureter fail to shift anteriorly from the cloaca before the urorectal septum grows down to divide the rectum from the bladder. If the ureter does not separate from the wolffian duct as usual, it may open into the organs developed from the wolffian duct—in the male, vas deferens, seminal vesicles, ejaculating duct; in the female, Gartner's duct.

It will be attached to the uterus and vagina if it does not remain isolated from the Müllerian duct. If the ureter is not detached from the wolffian duct after the sixth week of embryonic life it may be found opening into the urogenital sinus or the organs developing from this—the ureter in both sexes and the vestibule of the vagina in the female (Kelly and Burnam).

MOVABLE KIDNEY

(*Ren Mobilis, Wandering Kidney, Floating Kidney, Nephroptosis, and Dislocated Kidney.*)

Although Langdon formerly maintained that the normal kidney is absolutely fixed, it is now generally agreed that it has under normal conditions slight motility in three directions, longitudinal, anteroposteriorly and around the axis of its pedicle. The up-and-down movement with respiration and with body position is the greatest and varies within narrow limits, according to different authors. Thus, Piersol says that this movement does not much exceed 2 cm. (.8 in.); Harris says that it varies from 2 to 4 cm.; while Kelly and Burnam state that the longitudinal motility is from 2 to 5 cm. The other movements are very slight. English observers, especially, formerly applied the term "floating kidney" to such as had a mesonephron by which it hung out into the abdominal cavity. Now, any kidney which exceeds the normal motility is designated a movable kidney. With the patient in the dorsal position, the kidneys as a rule cannot be palpated. The right occasionally, and both in emaciated individuals may sometimes be felt. In the left lateral position, the right kidney may be palpated in most women, but not in men.

Various observers have arbitrarily classified the degrees of motility. Hilbert recognized two stages: first, the palpable kidney, in which the lower pole or less than the lower half can be felt; second, the movable kidney, in which the whole kidney can be felt and isolated with the fingers. Glenard recognized four stages. The first corresponded to the first stages of Hilbert; in the second the whole kidney may be felt, but the fingers cannot be inserted above the upper pole; in the third, the kidney may be "captured"; in the fourth, the kidney floats independently of respiratory motion. A useful classification is into three stages. The "palpable kidney," which may just be felt; the "movable kidney," which may be captured; and the "floating kidney," which may be moved to the brim of the pelvis or beyond the median line of the abdomen.

Etiology.—Movable kidney occurs quite frequently in women, being variously estimated from 4.41 to 56 per cent. of all women. It is much more frequent in women than in men, about 1 to 6, and is about 13 times more frequent on the right side than on the left. Considerations of the factors which hold the kidney in its normal position will explain the cause of its occurrence. These are (1) special body form; (2) the perirenal fascia in conjunction with the peritoneum; (3) the peritoneum, when this exists as a covering; (4) the renal vessels; (5) intra-abdominal pressure; and (6) the shape of the renal fossæ. There has been for a long time and still is considerable discussion as to which of these is the most important causative factor. Harris in a very careful and apparently convincing study arrived at the following conclusions: (1) The essential cause of movable kidney lies in a peculiar body form; (2) the chief characteristic of this body form is a marked contraction of the lower end of the middle zone of the body with a diminution of this portion of the body cavity; (3) this diminution in the capacity of the middle zone depresses the kidney so that the constricted outlet of the zone comes above the center of the organ and all acts such as coughing, straining, lifting, etc., which tend to adduct the lower ribs, press on the upper pole of the kidney and crowd it still further downward; (4) it is the long-continued repetition in suitable body form of these influences, which collectively may be called internal traumata, that gradually produces a movable kidney; and (5) a distinctly movable kidney is never the immediate result of a single injury or external trauma. In this last proposition Harris is supported by Sulzer, Budinger and Gutterbach. Kelly and Burnam, while not attaching the same importance to peculiar body form as Harris, Becker and Leunoff, sum up a discussion of the etiology in these words, "Movable kidney then seems to depend upon a number of predisposing causes. The predisposing causes are especially body form and laxness of the supporting structures of the kidney. The actual causes are various acute and chronic traumata."

Symptomatology.—No symptoms at all occur in the majority of cases. Kelly estimates that only 1 in 10 are accompanied by symptoms; Brewer 1 in 11; while Curschman found symptoms in 68 of 270 cases. The severity of the symptoms is not proportional to the degree of displacement. Edebohls has observed that the severest pain is associated with movement of from 4 to 10 cm. (1.6 to 4 ins.).

PAIN.—There are two main conditions upon which pain in movable kidney depends, and accordingly as one or the other of these is operative we will have two groups of cases with reference to pain. The first group is due to traction upon and irritation of nerves by the displaced kidney. Actual pain is not a prominent feature of this group. The patient is more likely to complain of an almost unendurable sense of weakness in the abdomen. There is rarely local pain in the kidney region. As the result of the irritation of the lumbar plexus, pain and discomfort may be complained of in the distribution of the branches of this plexus. Thus through the eleventh and twelfth dorsal, the ilio-inguinal, the iliohypogastric, the obturator, the crural and sciatic nerves, pain may be referred to the lower abdominal wall, the outer and inner side of the thigh, the genitals, the knee and the heel. Through traction on the diaphragm pain may be referred to the shoulder through the phrenic and supra-acrominal nerves. According to Kelly, these referred pains are not of very frequent occurrence. Pains with the characteristics of biliary colic may be present, due to the pressure of the right kidney upon the common bile duct. True reflected pain is rarely present in this group. These pains are increased by the erect posture and exercise, in some cases by menstruation, upon removing the corset at night, by constipation, by pregnancy, although McAlister states that they sometimes disappear in pregnancy. Generally they are relieved or mitigated by rest, lying down.

In the second group pain is a more prominent feature and is due to kinking and twisting of the renal pedicle. If only the vein is obstructed, the pain has the characteristics of that of passive hyperemia of the kidney and is due to the stretching of the kidney capsule. The pain in the lumbar region is dull, gradual and heavy, although, if the obstruction is sufficient to produce hematuria, the pains may resemble those of renal colic. If the ureter is obstructed, the pains are more severe and are due to the resulting hydronephrosis. Not infrequently the syndrome described by Dietl in 1864 is observed and is known as Dietl's crisis. The pain in the abdomen is severe, radiating to the lumbar region and along the course of the ureter. They are accompanied by nausea and vomiting and sometimes by symptoms of collapse. Not infrequently there is a rise in temperature, and palpation will elicit tenderness over the kidney and in the abdomen. Swelling of the kidney is rarely so great as to be recognized by palpation. During the attack, there is usually oliguria and sometimes a reflex anuria is present. The attack lasts from 6 to 48 hours and is followed by a transient polyuria. The attack may occur immediately after the obstruction or only when the hydronephrosis has reached a certain degree. They usually come on after excessive or violent motion.

In this group, contrary to the other, true reflected pain is met with. These may be complained of in the kidney zone of the affected or the opposite side. The disturbance in the kidney is transmitted through the sympathetic to the tenth, eleventh and twelfth dorsal and first lumbar segments of the cord and the pains are complained of in the distribution of the cerebrospinal nerves arising from these segments on the same or opposite side.

Pain in movable kidney may also result from associated conditions such as calculus, pyelitis, tuberculosis and inflammation of the kidney.

GASTRO-INTESTINAL SYMPTOMS.—Symptoms on the part of the stomach are quite frequent, especially the symptoms of so-called nervous dyspepsia, gastric pain, anorexia, nausea and vomiting. These symptoms are frequently attributed to nervous origin, but Kelly is inclined to refer them to the mechanical action of the displaced right kidney on the stomach for the following reasons: first, they occur most frequently with movable right kidney; second, suspension of the right kidney usually relieves the symptoms; third, suspension of the left kidney does not.

Frequently these symptoms are due to the associated splachnoptosis. Owing to the lack of mesentery in the second portion of the duodenum it is prevented from moving downward when it is dragged upon through its areolar tissue connection with the displaced right kidney and consequently it is stretched so that its lumen is diminished, giving rise to symptoms of the secondarily dilated stomach. These may be the symptoms of acute or chronic dilatation.

According to Bryan, the dislocated right kidney increases the dependent loop formed by the junction of the ascending and transverse colon, producing engorgement of the caput coli with the following resulting symptoms: pain, discomfort and heaviness in this region; a boggy tumor; febrile reaction; flatulence; and chronic constipation alternating with acute diarrhea. If the dislocated kidney constricts the superior mesenteric artery the symptoms of mucous colitis may be present. Symptoms of intestinal obstruction have been observed as a result of pressure of the displaced kidney on the intestinal tract. According to Edebohls, symptoms of appendicitis are frequently associated with movable kidney and he thinks that they are due to the pressure of the kidney on the superior mesenteric vein, thus interfering with the return flow of blood from the appendix.

GALL-BLADDER SYMPTOMS.—As a result of the traction and pressure upon the common bile duct by the movable kidney, the passage of bile is interfered with, giving rise to typical attacks of biliary colic. There is the severe pain, with its more or less characteristic distributon, assocated with nausea and vomiting and sometimes with a transient jaundice. However, these symptoms in movable kidney are rare and, according to Kelly, injection of the renal pelvis with sterile solutions does not reproduce the pain.

GENITO-URINARY SYMPTOMS.—Symptoms of pelvic congestion, as leukorrhea, dysmenorrhea, and intermenstrual pain are often observed in movable kidney. As Goelet has observed these symptoms in 75 per cent. of cases, he is inclined to refer the pelvic congestion to the displaced kidney. Schede reports a case in which both ovaries and uterus were removed without relief of the symptoms, which were subsequently relieved by anchoring the kidney. According to Kelly, the symptoms, except dysmenorrhea, are rare and are to be attributed to associated disturbance of the pelvic organs such as retroflexion of the uterus.

Pollakiuria is frequent during attacks of Dietl's crisis, but other manifestations on the part of the bladder are due to other causes than those dependent upon movable kidney. The urinary findings are normal in uncomplicated movable kidney. Oliguria followed by polyuria is frequently observed as the result of transient hydronephrosis produced by obstruction of the ureter by the displaced kidney. When the vein alone is obstructed, oliguria may result from passive hyperemia of the kidney. Hematuria may result from interference of the return flow of blood by obstruction of the renal vessels and ureter. The hematuria may be slight or marked, intermittent or long-continued. It is, however, not sufficient to give rise to the signs of a severe secondary anemia. Kelly would seem inclined to discredit macroscopical hematuria to movable kidney and if no other cause can be discovered to refer it to the essential hematurias. The following case of long-continued intermittent hematuria seen in consultation with Dr. George Livermore, who furnished the main data obtained in the case, would seem to the author to be due to a movable kidney. The patient was a young married woman, nullipara. The symptoms in the main were pains in the right side and lower abdomen, no distinct colic and general nervousness, associated with several attacks of intermittent hematuria, the last attack having continued for several weeks. Physical examination showed the young woman with nutrition below par and a movable right kidney of the first degree. The blood did not show a very marked degree of anemia, Hgb. 70 per cent. There was no leukocytosis. X-ray examination was negative for calculus. Cystoscopic examination revealed normal bladder and ureteral orifices. Ureteral catheterization with the subcutaneous injection of indigocarmin showed the time of appearance of the dye about the same on both sides. The urine from the left kidney was clear, contained no albumin, no blood and no casts. That from the right kidney was bloody, contained albumin, red blood-cells and casts. Careful examination of same did not show tubercle bacilli and animal injection of same gave negative results. Under absolute rest in bed and stypticin all symptoms, including the hematuria, promptly disappeared.

Albuminuria alone or accompanied with cylindruria occurs in movable kidney associated with obstruction of the vein or of the renal vessels and ureter, and disappears with the relief of the obstruction.

Reports of the results of modern tests for renal function in the movable kidney are meager. In uncomplicated cases there is usually no difference in the time of appearance of injected dye on the two sides.

NERVOUS SYMPTOMS.—In the absence of local symptoms referable to the displaced kidney, nervous symptoms are usually absent. With these, however, they are quite frequent. They consist of general nervousness and of the symptoms of neurasthenia and hysteria. They are due to nerve irritation and the mental disturbance as a result of the knowledge of the presence of a movable kidney.

REFLEX FUNCTIONAL SYMPTOMS.—Symptoms on the part of the circulation, respiration and sensation may be met with as the result of reflex functional disturbance.

PHYSICAL EXAMINATION.—Inspection in these cases will usually show a condition of nutrition below par. This is not the result of the kidney condition, but rather one of the predisposing causes frequently present.

Not infrequently will movable kidney be present in well-nourished patients. Mensuration will show a peculiar body form in these cases, which is also a predisposing cause rather than the effect of the movable kidney. According to Harris, the body cavity is divided into three zones; the upper being limited below by a horizontal plane at the level of the lower end of the sternum; the middle by one at the level of the tenth rib; and the lower zone, embracing all of the body cavity below this latter boundary. A diminution in the capacity of the middle zone will be found in all cases. The capacity of this zone is best estimated, according to Harris, by dividing the middle lateral diameter by the upper lateral diameter and multiplying the result by 100. The middle lateral diameter is obtained by measuring with calibrated callipers the greatest distance between the lower borders of the tenth ribs on both sides; the upper lateral diameter by determining by the same method the greatest distance between the lower borders of the seventh ribs. The normal index is 81.8 cm. Values for the index above this figure indicate the diminution in the capacity of the middle zone and will be found in all cases of movable kidney.

Palpation will in the greatest number of cases reveal the presence of a movable kidney. There are three methods in use in performing palpation. The dorsal method was first popularized by Frank. The patient lies on the back with the knees drawn up and thigh flexed on the abdomen to relax the muscles of the abdominal wall. The examiner stands at the side of the kidney to be examined, with the left hand in the flank and the right hand on the abdominal wall over the kidney. The patient is requested to breathe deeply and the kidney is felt best by the posterior hand as it descends and ascends with inspiration and expiration. The lateral position is known as Israel's method. To examine the right kidney the patient is in Sim's position, the examiner is on either side of the patient with one hand in front and the other in the back. The patient breathes deeply and the kidney is best palpated by the hand in front. To examine the left kidney the positions are reversed. The examination by this method will be positive more frequently than by the dorsal method. A third method is the use of the erect position. The patient places the foot on the side to be examined on a stool and bends the body slightly to the same side. This method will sometimes give positive results when the other methods fail. If the kidney is only slightly movable, a smooth rounded body will be felt. When quite movable the kidney can be grasped between the hands, and its outline be made out. Firm pressure will cause the patient to complain of a sickening sensation. In some cases the pulsation of the kidney vessels may be detected. The slipping back of the kidney with each expiration is quite characteristic. Percussion is practically of no value to determine the presence of a movable kidney.

Diagnosis.—There is no diagnostic syndrome of symptoms for nephroptosis. Examination by the x-ray may confirm the results of palpation and sometimes show abnormal motility where the latter method is negative. It will also accurately determine the degree of motility. The pelvis of the kidney is injected with thorium X and one plate exposed with the patient in the prone position and a second one with the patient in the erect posture. The different positions of the kidney will be readily shown. With the presence of a movable kidney it becomes important to determine whether the symptoms presented by the patient should be referred to the kidney. For this purpose Kelly has suggested the injection of the pelvis of the kidney with colored sterile solution, being careful to use a large ureteral catheter to prevent back-flow. He states that this method will reproduce the pain complained of by the patient either in the presence or absence of a hydronephrosis.

Other conditions may produce symptoms similar to those produced by movable kidney and will have to be differentiated from it. Sciatica may have to be differentiated. In movable kidney the pain is not limited to the sciatic nerve; the anterior crural is often involved with it; the sciatic is not painful to pressure, is accompanied by a desire to urinate, and is not influenced by exposure to cold and dampness; there is no loss of motor power or atrophy of the muscles; it is increased by exercise and relieved by rest in bed, and is not prone to nocturnal exacerbations; there are digestive disturbances associated with exercise and jolting; there are intervals of complete rest and comfort; and there is temporary relief from medicinal measures for the digestive disturbances associated with absolute rest in bed.

The tumor presented by a movable kidney may have to be differentiated from hydrops of the gall-bladder; the kidney outline may be made out on palpation; there is no tenderness on pressure in movable kidney unless the kidney is diseased; movable kidney has a wider range of movement and when released has a tendency to return to the right lumbar region.

The pains of movable kidney may be differentiated from those due to chronic appendicitis by establishing the presence of abnormal motility by palpation or the x-ray, and the reproduction of the pain by injecting the pelvis of the kidney. Both conditions, however, frequently coexist.

Movable kidney is differentiated from tuberculosis of the kidney by the following findings in the latter: slight hematuria, pyuria, polyuria and the presence of tubercle bacilli in the urine; frequent painful urination, with irritation of the ureteral orifice on the affected side; the evidence of tuberculosis elsewhere.

It is differentiated from nephrolithiasis by the x-ray which will in the majority of cases show the stone, the ureteral orifice diseased and an increased number of urine shoots. In the movable kidney there is sudden diminution of urine, sometimes with the coincident appearance of hematuria and blood casts, and increased vascular tension with enlargement of the kidney.

Diseases of the stomach may have to be differentiated by careful special examination directed to this organ.

Among the complications of movable kidney may be mentioned hydronephrosis, passive hyperemia and atrophy of the kidney, adhesion of the kidney to the anterior edge of the right lobe of the liver, hydrops of the gall-bladder and dilatation of the stomach.

It is frequently associated with other conditions, among which may be mentioned deformities of the liver, splanchnoptosis, hernia, misplacements of the uterus, appendicitis, nephrolithiasis, pyelitis, tuberculosis of the kidney and nephritis.

Treatment.—Patients possessing the peculiar body form of movable kidney should be advised as to certain prophylactic measures with respect to the avoidance or correction of certain conditions which are known to act as predisposing causes in the production of movable kidney. They should be advised to take **exercises calculated to strengthen the body wall.** They should be **advised against** wearing **tight bands** about the lower chest, and women especially **against tight lacing.** The body should be kept in a good state of nutrition by the proper attention to **diet, personal hygiene** and **exercise.** In these cases careful attention should be paid to care of these patients in labor and during the puerperium.

Possibly not more than 20 per cent. of these patients complain of symptoms, therefore the great majority of them present a condition to which the old saying "where ignorance is bliss, 'tis folly to be wise" is most appropriately applied. Unless the physician is quite sure that the symptoms complained of are due to the displaced kidney, he should exercise great care not to acquaint the patient with the knowledge of its existence. If a movable kidney with symptoms exists in a patient who is undernourished, measures directed to the improvement of nutrition should be carried out. (See treatment of Neurasthenia.) Symptomatic treatment is frequently necessary. The group with slight degrees of pain and digestive disturbances will usually be relieved by **rest in bed** and **mechanical support.** The severe pains of Dietl's crises will often require rest in bed and the hypodermatic administration of **morphin sulphate,** grain 1/8 to 1/2 (.008—.0324 gram); slight pains with hematuria, rest and **stypticin,** 1/2 grain (.0324 gram) by mouth every 4 hours, continued for a day or two. Mechanical therapy by **belts** or **bandages** should be tried in every case of movable kidney. The results of this method of treatment are variable. It would seem to depend upon the kind of case and the observer, and unfortunately the kind of practice the latter is engaged in would seem to influence the result. Thus Morris, Edebohls and Harris regard it of little value, while Glénard thinks it is very effective; C. D. Aaron has reported 95 per cent. of cures in 414 cases and Sailer has never seen any good from surgical procedure. There are two principles to be observed in the application of the bandage. It should give support to the entire abdominal wall, bringing pressure to bear from below upward, and produce pressure immediately below the kidney to prevent its coming down. This can best be accomplished by the coöperation of the physician and the bandage maker. The bandage should be applied with the patient in the lying posture and worn continuously when she is moving about. The question of whether **surgical treatment** is necessary will often have to be considered by the general practitioner or internist. Each case will have to be considered and the indications for operation are very fairly presented by Kelly and Burnam. In general, it would seem better to advise patients, who cannot afford the "rest cure" or who object seriously to wearing bandages, to be operated upon. This advice should also be given in cases in which a thorough trial of general measures combined with mechanical therapy fail, and the same in cases having frequent attacks of Dietl's crises. It is possibly better not to advise operation in cases associated with general visceroptosis. **Nephropexy** with the obliteration of the renal fossæ is generally regarded as the operation of choice.

Pathology.—The kidney is normal in the majority of cases. Fetal lobulation has frequently been noted. Hydronephrosis is frequently present and if it has existed a long time may lead to atrophy of the renal parenchyma. The right kidney has been found adherent to the liver. There is occasionally dilatation of the stomach and appendicitis is frequent. Deformities of the liver are often present, the result of tight lacing, and biliary stasis and hydrops of the gall-bladder may be present.

Historical Summary.—While movable kidney had been noted earlier by François Perdemontanous (1581), Riolan (1682), Pierre François Olive Rayer in his three-volume treatise on disease of the kidney, one of the epochal works in the history of these diseases, discussed movable kidney in all of its phases. The next notable contribution to the history of movable kidney was made by Dietl in 1864. Much discussion arose as to whether movable kidney existed independently of a general splanchnoptosis. Glénard maintained that it did not. In this view he was supported by Israel in Germany and Tuffier in Paris. The preponderating evidence, however, from kidney surgeons in America, England, France, and Germany is in favor of the opposite view. The first nephrectomy for movable kidney was performed by Gilmore, of Mobile, Ala., in 1870. This operation does not, however, now have the popularity of nephropexy which was introduced by Halen of Germany in 1881.

UREMIA

Definition.—The term uremia includes various symptom complexes presumably due to different causes such as toxemia and circulatory disturbances associated with diseases of the kidney and obstructive diseases of the urinary passages. It occurs most frequently in inflammatory conditions involving the kidneys, in bilateral surgical diseases of the kidney, and in conditions associated with anuria. It includes symptoms referable to the nervous, respiratory, circulatory, and digestive systems. All of these manifestations are very rarely present in any one case. The symptoms may occur at intervals or may be entirely latent.

Symptomatology.—NERVOUS SYSTEM.—*Convulsions* have been long regarded as among the most prominent manifestations of uremia. Pure eclamptic attacks are, however, relatively infrequent. Among 50 cases occurring in the Memphis General Hospital and private practice in the last two years, there have been 8 cases. Of convulsive types of uremia, the eclamptic or epileptiform attacks are most frequent. They simulate very closely true epilepsy. Auræ may or may not be present. They may come on suddenly or be preceded by prodromal symptoms such as headache, drowsiness, stupor, dizziness, disturbances in the auditory and visual apparatuses or in the digestive system. The epileptic cry is usually absent. Tonic are succeeded by clonic convulsions. Usually there is sudden loss of consciousness during the attack, though it may be retained throughout. The convulsions are followed by a variable period of coma, or only a condition of somnolence may be present.

During the tonic stage, as a result of the involvement of the muscles of respiration, there may be marked cyanosis, turgidity of the veins, while during the succeeding clonic stage the tongue may be bitten. Not infrequently there is involuntary passage of the urine and feces. The respiration is embarrassed; the pulse, which before the attack is often tense and slow, during the attack is small, quickened, and often irregular, after the attack again becoming tense and slow. The blood-pressure is raised and, according to Ascoli, has a tendency to rise during the attack. Usually there is slight elevation of temperature. In this variety of uremia the pupils are most frequently dilated. The convulsive attacks may simulate jacksonian epilepsy, or the convulsions may be tetanic or choreiform in character, or the attack may set in with sudden coma without convulsions.

Instead of the eclamptic attacks various symptoms on the part of the nervous system occur which have been designated by some authors as *eclamptic equivalents.* Among these are *paralyses* of various kinds. There may be *hemiplegia* or monoplegia. The hemiplegia may be associated with aphasia or the latter may occur independently. *Amaurosis* is not rare; *hemianopsia* is less frequently present, and *color blindness* has been reported. Disturbances in the auditory apparatus occur. These may be of an irritative character, such as ringing and buzzing noises in the ear; or of a paralytic nature, varying from difficulty in hearing to complete deafness. Increased reflexes, Babinski and Kernig's phenomena, and stiffness of the neck may be present singly or collectively. Among these may also be included headaches, frequently in form of migraine, dizziness, fainting attacks and various mental disturbances. The latter are variable; there may be only delirium associated with aphasia; or the patient may be irritable, restless or aggressive, or there may be depressive illusions or hallucinations which render the patient melancholic, and have been known to result in suicide. Certain characteristics help one to recognize these various symptoms or eclamptic equivalents as uremic. They occur quickly, run their course proportionately rapid; the paralytic phenomena may be associated with regional convulsions, which may occur first on one side of the body, then on the other; finally they all improve with improvement of the associated diseases.

Death may occur in the first eclamptic seizure, though it usually does not do so. The attacks show a great tendency to recur and frequently after repeated attacks death ensues. Although there are many theories as to the cause of the symptoms thus far described, it must be acknowledged that little is definitely known. Ascoli was able to produce convulsive seizures by the injection of nephrolysins into the subarachnoid space of certain animals and believed that such symptoms as above described were due to the nephrolysins arising from the destruction of kidney tissue in diseases of the kidney. The facts that eclamptic attacks were associated with increased cerebrospinal pressure and that the symptoms improve on lumbar puncture and limitation of salt and water and grow worse with a free salt and water intake, led Volhard and Fahr as well as other authors to refer the symptoms of the eclamptic attack to edema of the brain which is about the only lesion which can be demonstrated in this organ in cases coming to autopsy. Widal has referred the attacks to the impregnation of the cerebral and bulbar centers with sodium chlorid (chloruremia). Vaquez and others think they are due to a spasmodic contraction of the brain vessels as a result of the over-production of adrenalin. N. B. Foster has isolated a crystalline toxic substance from the blood of patients with eclamptic uremia. This substance was found to be rapidly fatal to guinea pigs and he thinks may be the cause of the convulsive attacks.

The eclamptic equivalents have been referred to vascular spasm on an arteriosclerotic basis (Forlanini, Pal, Vaquez, Osler). Here may be included also such symptoms as sensations of cold, paresthesia, dead fingers and toes due to vascular cramp as a result of arteriosclerosis of the arteries of the extremities and usually regarded as uremic. Still, most authors assume in addition the action of some toxic substance.

Digestive System.—Scarcely less important than the symptoms referable to the nervous system are those due to disturbances in the alimentary tract. Among these are anorexia, nausea, vomiting, hiccup, stomatitis, and diarrhea. These may occur on a functional or an anatomical basis. Catarrhal and ulcerous stomatitis, hemorrhagic erosions of the stomach and intestinal ulcers have been described.

Inflammations of the serous membranes, pleurisy and pericarditis, and inflammations of the skin frequently occur as terminal events in kidney disease and have been regarded as manifestations of uremia. Ascoli's view that these conditions are to be considered uremic only in so far as the kidney disease and the uremia destroy the resistance of the tissues is now generally accepted. The same obscurity with respect to the real cause maintains here as in the other manifestations of uremia.

Respiratory System.—Dyspnea is a symptom which frequently occurs in renal disease and may be the result of different causes or conditions associated with the kidney disease, such as emphysema, bronchitis, cardiac failure, pulmonary edema, pneumonia, hydrothorax and hydropericardium. In contradistinction to the dyspnea arising from these causes, periodic asthmatic attacks associated with hypertension and the periodic dyspnea of the Cheyne-Stokes' type are regarded as uremic. Hyperpnea may also be present and is referred to the acidosis which not infrequently is present in the uremic state.

Symptoms Due to Urinary Poisoning.—Besides these symptoms another group is present in uremia and has been referred to urinary poisoning by Ascoli and others. These include great mental and bodily weaknesses, apathy, stupor, inability to sleep soundly, labored and sighing respiration, dyspeptic symptoms, urinous odor of the breath, jerking of muscles and tendons, and fall of temperature; frequently they end in sudden cardiac failure.

Functional Tests.—Functional kidney tests give very variable results in the different manifestations of uremia. In the eclamptic attacks associated with the acute and the second stage of diffuse glomerulonephritis, and in the eclamptic equivalents associated with hypertension of sclerotic conditions there is usually very little evidence of kidney insufficiency as indicated by the tests now used to determine the functional capacity of the kidneys. The non-protein nitrogen and urea in the blood are within normal limits; notwithstanding this, the urea index and Ambard's coefficient may show slight impaired functional capacity of the kidney.

Reiss states that there may be no evidence of salt retention even in exact metabolic studies of these cases, though the kidney test-meal may show low salt concentration and the phenolsulphonephthalein excretion in two hours may be slightly lowered. According to Reiss, there is no evidence of molecular concentration or increased osmotic tension in the blood. These statements may be illustrated in the following cases:

S., with a case of acute glomerulonephritis plus nephrosis, was attacked with convulsions followed by coma lasting forty-eight hours. The non-protein nitrogen of the blood showed 23.1 mg. per 100 c.c. blood.

G. M., with the second stage of glomerulonephritis, had convulsions, unconsciousness, delirium and great restlessness. The kidney test-meal showed a high fixed specific gravity of the day urine; a high specific gravity of the night urine; no night polyuria; a low salt concentration, day .093 per cent, night .55 per cent; a good nitrogen concentration, day 1.38 per cent., night 1.77 per cent.; and a phenolsulphonephthalein excretion of 45 per cent. in two hours.

In P., another case of chronic glomerulonephritis, with convulsions, coma, and dilated pupils, the kidney test-meal showed a good water excretion; a slight night polyuria, 624 c.c.; a low salt concentration, day .083 per cent., night .678 per cent.; a good nitrogen concentration, day .858 per cent., night 1.08 per cent.; and the non-protein nitrogen of the blood 28 mg. per 100 c.c.

B., probably with a case of benign hypertension with delirium, hallucinations and aphasia, showed a blood urea of .372 gram per liter; 12.61 grams of urea in twenty-four hours' urine; 6.6 grams of urea per liter of urine; a urea index of 32; an Ambard coefficient of .144; and a phenolsulphonephthalein excretion of 64 per cent. in two hours.

These cases are infrequent in comparison with those showing the symptoms of urinary poisoning, which according to some, especially Volhard and Fahr, deserve only the name uremia. In these there are marked evidences of serious impairment of kidney functions. There is marked retention of the Rest Nitrogen and urea, a low fixed specific gravity of the day urine, a low specific gravity of the night urine, low salt and nitrogen concentration, a low phenolsulphonephthalein excretion, a low urea index, a high Ambard coefficient, and increased osmotic tension of the blood. It must not be forgotten that convulsions, coma, and other cerebral symptoms may be combined with these cases. These functional tests may indicate impending uremia even in the absence of any symptoms of this condition, as in the following case which at the time of examination showed no symptoms at all indicative of uremia.

The functional tests showed a low fixed specific gravity of day urine; a night polyuria with low specific gravity; NaCl of day urine, .25 per cent., of night urine .3 per cent.; nitrogen of day urine .25 per cent., of night urine .288 per cent.; phenolsulphonephthalein 0 in two hours and a blood urea of 324 mg. per 100 c.c. Two weeks later the patient died with the mixed type of uremia, *i.e.*, symptoms of urinary poisoning and those of a psychotic nature and coma.

Clinical Varieties.—TYPES OF UREMIA.—Various classifications have been suggested for uremia. Rose Bradford and most authors of text books divide the manifestations of uremia into acute, chronic, fulminant, and latent forms. Ascoli, upon the basis of clinical observations, experimental results and theoretical considerations, recognizes two groups, *viz.*, renal uremia (*Nierensiechtum*) and urinary poisoning. The former includes increased blood-pressure, eclamptic attacks, stuporous and comatose conditions, mental disturbances, paralyses, disturbances of sensation, and amaurosis. In the latter Ascoli includes stupor, coma, a part of the mental disturbances, the weakened condition of the heart, the periodicity of the pulse and the breathing, the stomatitis and the conditions in general characteristic of chronic uremia.

Emil Reiss has classified uremia on a clinical basis into four forms:

(1) The asthenic form which is characterized by drowsiness and indifference, bodily fatigability, prostration, and sudden heart death. In the blood there is an increase of the non-protein nitrogen and osmotic tension.

(2) The convulsive or eclamptic form, characterized by the frequent occurrence of convulsive attacks which are extraordinarily similar to those of general epilepsy. Reiss also includes in this form paralyses. The external secretion of the kidney is perfectly intact.

(3) The psychotic form recognized by the predominance of psychical changes, at first marked confusion, hallucinations, illusions, later also deep coma, not only agonal. These conditions are mostly of a fleeting nature. There is in this form no retention of abnormal products of metabolism.

(4) The *mixed* form includes all of the symptoms occurring in the simple forms, often in a less typical manner.

Volhard suggests a three-fold classification: (1) The eclamptic type without kidney insufficiency, *i.e.*, without nitrogen and salt retention, but to be referred to edema of the brain; (2) the form with dyspeptic symptoms, twitching of the muscles and tendons, great fatigability, symptoms similar to those of urinary poisoning and associated with marked azotemia; and (3) the group including psychical disturbances, cerebral crises, transitory aphasia, paralyses, dizziness, headache, Cheyne-Stokes' breathing and nocturnal asthma.

These also are not associated with kidney insufficiency and by other authors are referred to angiospastic, arteriosclerotic, or cardiac origin and therefore designated as pseudo-uremia. It would seem that there is great advantage from a prognostic and therapeutic standpoint in classifying the manifestations of uremia into those with and without kidney insufficiency.

Treatment.—As will be seen from the foregoing, uremia is a complex condition due to different causes and associated with various conditions. This should be appreciated in the consideration of its therapy. While we recognize that these forms occur in various combinations, they frequently occur in pure types and it will be convenient to consider the treatment as applied to these types.

It is quite certain that eclamptic uremia frequently occurs independently of impaired kidney function, when it may be associated with acute glomerulonephritis, the second stage of chronic glomerulonephritis (chronic glomerulonephritis without kidney insufficiency), or with benign hypertension. Whether it is due to nephrolysins, edema of the brain, or a crystalline toxic substance, in all of the above-named conditions increased blood-pressure and slight dropsy predispose to the development of convulsions. The indications are plain and the carrying out of these is frequently followed by very gratifying results. Called to a patient developing uremic convulsions suddenly, the so-called acute uremia, the following measures should be resorted to at once:

(1) **Venesection.**—If the patient is plethoric, 500 or 600 c.c. of blood should be removed from the median basilic vein. Of course, if the patient shows evidence of cardiac weakness or is a child, much less should be withdrawn.

(2) This procedure should be followed immediately by a **lumbar puncture.** The amount of cerebrospinal fluid withdrawn will be governed by the pressure; frequently 30 or 40 c.c. will be obtained under markedly increased pressure.

(3) Thirty grains (1.95 grams) **chloral hydrate** should be administered by rectum.

If it has not already been done, **functional kidney tests** should be performed. The presence of albumin and casts are not of much help to us; they occur with convulsive seizures due to any cause. The **phenolsulphonephthalein test** should be made. Unless the output is below 40 in two hours, it is not likely that the blood urea will be increased. The "**phthalein**" **test** is simple and can be carried out by any physician at any place. While Marshall's method has greatly simplified the determination of the blood urea and should be done by the physician in his office, the general practitioner usually has not the necessary equipment to do this. Usually, however, the results of both tests will be found within normal limits. The effects of these procedures are a temporary fall in blood-pressure, and a subsidence of the convulsions followed by a variable period of coma. If there is a tendency for the convulsions to return the chloral may be repeated by rectum. The author does not think that severe purgation is to be desired and has never used croton oil, which has been so frequently resorted to in these conditions.

If the patient's bowels have not moved freely, a **mild purgative** may be given. While some authors state that mercurials are contra-indicated in uremia, the author's preference is for one of the mercurials. If the patient has regained consciousness sufficiently to swallow, **massæ hydrargyri**, grains 10 (.67 gram), **extractum Hyoscyami**, grain ½ (.03 gram), may be given in capsule. If the patient is still comatose, 10 grains (.67 gram) of **calomel** may be swallowed if placed with a spoonful of snow ice on the back of the tongue. Usually there is no indication for a low protein diet, but the **salt and fluids should be restricted.** If the patient soon regains consciousness, an ordinary **light diet, salt free**, with not more than 48 ounces of fluids in the twenty-four hours, may be allowed. If unconsciousness continues for some time and nourishment be deemed necessary, one pint of a 10 per cent. solution of glucose in plain water to which 2 drams (7.8 grains) of **sodium bicarbonate** may be added can be given by proctocylsis every eight hours. If after the patient clears up, there is a recurrence of the convulsions in a few days and the patient's condition seems to contra-indicate another venesection, this may be substituted by 5 minims (.3 c.c.) **tincture of Veratrum viride**, repeated as often as necessary and the other measures repeated. The further treatment will depend upon the associated kidney condition (*q.v.*).

ECLAMPTIC EQUIVALENTS.—In the course of benign hypertension and the combination form of sclerosis with nephritis, various vascular symptoms referable particularly to the nervous system and usually regarded as uremic demand treatment. As stated above, these eclamptic equivalents include transitory paralyses, disturbances in vision and hearing, paroxysmal dyspnea and Cheyne-Stokes' respiration, increased reflexes, headache and vomiting, sometimes associated with fainting attacks and psychical disturbances. Whether the transitory paralyses are to be referred to vascular crises on an arteriosclerotic basis, to localized edema, or to punctate hemorrhages or to the toxic influence associated with these, the chief indication is to lower the blood-pressure. Vasodilators have met with little success in the treatment of these symptoms. With the occurrence of transitory paralyses the patient should be put to bed and his diet limited. As a rule, the benign hypertonic is not anemic and venesection, which in these cases may be resorted to without misgivings, is one of the most valuable measures. In the cases of the combination form of sclerosis with nephritis which are more likely to be associated

ıwal of large quantities
d.
ature, especially in the
in part dependent upon
by the kidney. Mariott
ult from an increase of
lministration of calcium
perience the administra-
ie relief of these uremic
strongly the **inhalation**
however, **morphin** hypo-
r the severe headaches
neningismus, the **ice-bag**
r **products**, and **acetyl**
nbar puncture which is
be tried.
lute quiet, a **darkened**
otect the patient against
g sheet may have to be
will often induce sleep.
s been recommended in
s for the insomnia asso-

ue Uremia.—This form
age of chronic glomeru-
aneway has stated, the
purely symptomatic and
definite about the toxin
oms of true uremia, we
on of waste products of
ability of the kidney to
of these products the
ng time by a compensa-
fore to lower and main-
of the end products of
the non-protein nitro-
intain the compensatory
ication may be met with
tein intake and sparing
The second indication
ich will be successful in
y left.
toms usually present as
the patient may render
ith difficult. The author
diet of Chace most use-

has

ful in these severe [illegible] juice from one lemon, two-thirds of a cup of water, one teaspoonful of cane sugar, and six table-

Therapeutic Uses: Clinical experience has fully confirmed the observations of animal experiment. The average dose for man is 0.2 gm., and this as a rule brings on sleep within about an hour, the sleep being very tranquil and deep, lasting for six or seven hours. The patient awakes feeling rested and refreshed. No unpleasant by-effects have been reported to follow the use of the drug, and the fact that it does not develop any cumulative action has been pointed out as a special feature in its favour. This, by the way, is additional proof of its rapid destruction within the body and of its prompt excretion.

The following are appropriate doses: —
Nervous Sleeplessnes – 0.2 gm., rarely 0.3 gm.
Nervous Disturbances, Depressional States, etc. – 0.1 gm. several times during the day.
Excitation – minimum dose – 0.5 gm.

This last dose – 0.5 gm. – has been found to induce sound sleep in severe psychical conditions. Phanodorm is best taken in a sufficiency of some hot liquid.

PHANODORM

in supplied in bottles of 10 and 25 gm. (powder) and in tablet form in tubes of 10 tablets of 0.2 gm. (gr. 3).

Bibliography:

Impens E.: Medizin. Klinik, 1925, No. 18.
Isaac-Krieger, K. u. *Noah, G.*: Medizin. Klinik, 1925, No. 18.
Wiebeck u. *Tetsner*: Münch. med. Wochenschr., 1925, No. 23.
Mayer, W.: Klin. Wochenschr. 1925, No. 23.
Fünfgeld, E.: Klin. Wochenschr. 1925, No. 29.
Müller, P.: Münch. med. Wochenschr., 1925, No. 35.
Lackerbauer, J.: Zeitschr. f. d. ges. Neurol. u. Psychiatrie. 1925, Bd. 99, No. 1/2.
Pfannmüller: Münch. med. Woch., 1925, No. 46.

E. MERCK Chemical Works **DARMSTADT**

A. 2258/110430 e.
Printed in Germany
Pha. 3/30.

spoonfuls of lactose, four times a day. This will furnish about 1242 calories, approximately .8 gram of iron and an alkaline ash. Chace states that a patient can maintain himself on this diet three or four days without drawing on his body protein. After this, or before if possible, the above diet may be **substituted by the following**: Morning and evening 300 grams of ripe bananas and 100 c.c. cream; at noon 200 c.c. plain cream soup, 300 grams of bananas and 200 c.c. milk. This affords 1335 calories, 29 grams of protein or approximately 45 grams of nitrogen and an alkaline ash. Care should, however, be taken not to continue these very low diets too long because the strength of the patient will require protection, as marked asthenia is one of the chief features of this form of uremia. If the condition of the patient is such that the diet cannot be taken by mouth, 10 per cent. glucose may be administered by proctocylsis. Frequently, however, this cannot be retained per rectum, in which case it may be administered by **stomach tube**. It has long been recognized that a marked diminution of the quantity of urine in chronic nephritis without an increase in specific gravity is a forerunner of uremia. More recently Foster has shown how an increased water intake will increase the elimination of nitrogenous products. Still, Schlayer's observation that in nephritis the kidney may become fatigued when overstimulated and instead of responding with an increased diuresis may answer with diminished elimination, must not be forgotten. It is due to this fact chiefly that the more stimulating diuretics are contra-indicated in his condition. However, it is desirable that with the low protein high carbohydrate diet, 2500 or 3000 c.c. of water or fluids should be taken in the twenty-four hours. This may be taken in the form of pure water or ades by mouth, or soda, glucose or saline solutions by rectum. Cardiac embarrassment is the chief contra-indication to these measures.

Venesection is to be used here only after careful consideration of all the conditions present. On account of the anemia and weakened condition of the patients usually present, the ultimate harm which results will usually outweigh the immediate beneficial results. It has been proposed to overcome the undesirable results of venesection by blood transfusion or plasmaphoresis. Whether transfusion meets the difficulties has seemed questionable to the author, and he has obtained the impression that the severe reaction which frequently attends the citrate methods adds increased difficulties. Plasmaphoresis has so far met with little success. Elimination through other channels as by the bowel and skin is a time-honored indication in the treatment of uremia. Discretion is, however, to be used in the application of these measures also, as severe purgation and diaphoresis in the presence of the impaired function of the kidney may increase the concentration of the blood and increase the danger. Sufficient bowel movements may be secured by the administration of **compound Jalap powder**, dram ½ to 1 (2 to 4 grams), which may be supplemented by **irrigation of the colon with water** at 110° F. (43.33° C.). **Diaphoresis**, the beneficial effects of which are purely empirical, may be secured by the hot air bath, the brick method, electric light baths, hot packs and hot baths.

The severe gastro-intestinal symptoms which usually accompany this form of uremia are generally central or eliminative in origin and are best met by **lavage of the stomach and bowels** and general sedatives. Severe abdominal pain will sometimes require the hypodermatic administration of morphia. Associated conditions such as myocardial insufficiency and acidosis demand appropriate treatment. The uremia associated with obstruction of the lower urinary tract is best treated by the method of Young which consists of the introduction of a **retention catheter**, forced water intake up to 3 to 6 liters (3.17 to 6.34 quarts) per day and a low protein diet, followed by the **removal of the obstruction surgically.**

NEPHROPATHIES OF CIRCULATORY ORIGIN

The diseases of the kidneys of circulatory origin include anemia, hyperemia, embolism, thrombosis, and infarction of the kidney and arteriosclerotic processes of the kidney vessels.

The clinical symptoms and anatomical appearance attributable purely to anemia of the kidneys are so rarely encountered that it will be unnecessary to say more than that the condition occurs as a part of a general anemia from local causes which prevent an ingress of blood to the kidneys, and from spasmodic contraction of the arterial wall.

Active hyperemia of the kidney manifests itself clinically by backache, pollakiuria, and the passage of a small amount of urine which may contain albumin and a few casts. Independent of acute glomerulonephritis which it always accompanies, it may occur under a variety of conditions, as in acute infections, prolonged fevers, as a result of chilling of the body, and the irritant action of many drugs, as mercury, arsenic, antimony, potassium chlorate, turpentine, cubebs, capaiba, and cantharides.

Large hemorrhagic infarcts which result from the plugging of the renal vessels rarely occur. They may give rise to suddenly occurring hematuria accompanied by unilateral pain. The hemorrhage usually quickly disappears. These symptoms ensuing on the presence of heart disease will suggest the diagnosis.

More or less diffuse atherosclerosis of the small blood-vessels of the kidney will be described under the genetic term Bright's Disease. Chronic passive congestion of the kidneys and the focal atherosclerotic nephropathy will be described more fully here.

CHRONIC PASSIVE CONGESTION OF THE KIDNEYS

(*Stasis Kidney*)

Definition.—The clinical history and physical findings will depend upon the causative disease producing the myocardial insufficiency, the obstruction of the inferior vena cava above the renal veins or the obstruction of the renal veins themselves. Chronic passive congestion of the kidneys is most frequently associated with myocardial insufficiency which may be due to organic disease of the heart itself or to disease elsewhere in the body, to which the disturbance in the heart is secondary, *e.g.*, pulmonary emphysema, hyperthyroidism, atheroscelerosis and the chronic nephropathies.

Etiology.—Experimental works show the presence of two factors in the production of chronic passive congestion of the kidneys. The *feeble* arterial flow produces cortical and glomerular congestion and exudation of albumin into the capsule and lessened venous outflow produces engorgement of the medulla.

Symptomatology.—The cardiac decompensation may be *relative* or *complete.* In the former there will be shortness of breath which is brought on by exercise or it may occur after a heavy meal and is frequently associated with the excessive use of tobacco. The dyspnea frequently manifests itself in asthmatic attacks at night and is due to the more or less complete edema of the lungs which results from the early failure of the left ventricle in conditions like aortic regurgitation, sclerosis of the coronary arteries, benign hypertension, and sclerosis of the kidney vessels combined with nephritis. Cough is frequently present and may occur in paroxysms. A feeling of constriction in the chest, which sometimes amounts to pain, may be complained of. Certain movements of the body may produce dizziness. If carefully looked for, edema about the ankles may be discovered, and the patient not infrequently complains of edema in this area occurring during the daytime which disappears after a night's rest. Cyanosis may be present. Disturbances in sleep are common. The sleep is restless and disturbing dreams and nightmares frequently awaken the patient.

The symptoms of complete cardiac decompensation are more outspoken. The dyspnea is more severe and is present when the patient is at rest. While the mechanism of dyspnea in cardiac disease is not well understood, several causative factors have been suggested, as insufficient ventilation of the pulmonary alveoli, insufficient interchange of gases between the blood and the air in the alveoli, and retardation of the blood flow in the tissues and acidosis. Insufficient ventilation of the pulmonary alveoli is favored by several conditions which may be associated with or the result of cardiac decompensation, *e.g.*, pulmonary congestion, bronchitis, bronchopneumonia, pulmonary infarction, the enlarged heart, pericardial and pleural effusions, and interference with movements of the diaphragm by an enlarged liver or ascites. Von Basch attributed cardiac dyspnea to increased lung volume and diminished elasticity of the pulmonary tissue. Modern studies have, however, shown that there is no increased volume inasmuch as the residual air in cardiac decompensation is normal or only slightly increased and the mid volume of air is less. Still the diminished elasticity is shown by the diminution of the vital capacity which may be only 20 or 25 per cent. of the normal in these cases. Siebeck has called attention to the fact that ventilation is rendered more difficult by the fact that a large proportion of the inspired air is breathed out with the next expiration. The same author also found that the functional dead space is increased in heart disease. It has often been assumed that an insufficient interchange of gases between the blood and the air in the alveoli is a factor in cardiac dyspnea. Hürter has, however, shown that the oxygen of the arterial blood in cases of cardiac decompensation is over 80 per cent. of the normal capacity, and Hewlett suggests that the retardation of the blood flow through the tissues which results in an inadequate supply of oxygen to the tissues or inadequate removal of carbon dioxid from them is a more important factor in the production of dyspnea.

Lewis and his co-workers have called attention to the frequent association of cardiac insufficiency with acidosis which probably is renal in origin. Hewlett believes that while acidosis may be a contributing factor in the production of cardiac dyspnea, it is not the sole or the chief factor for the following reasons: (1) The degree of acidosis is rarely extreme; (2) equally marked degrees of acidosis in diabetes cause hyperpnea without dyspnea; (3) the administration of sufficient alkalies to cause an alkaline urine does not usually relieve the dyspnea to any material degree; and (4) no definite relation exists between the degree of dyspnea and the degree of acidosis.

Frequently patients with complete cardiac decompensation breathe better sitting up than in the recumbent posture, a condition designated as orthopnea. The sitting posture lowers the abdominal viscera which push out the anterior abdominal wall, thereby producing more favorable conditions for expiration. It also lowers the position of the diaphragm which increases the size of the lungs as well as the aperture traversed by the inferior vena cava, thereby favoring the return flow of blood from the lower parts of the body. In complete cardiac decompensation the cardiac asthma of relative insufficiency usually gives place to a stasis bronchitis. Though in complete decompensation paroxysmal attacks of difficult breathing frequently occur and are often associated with Cheyne-Stokes' breathing, McKenzie is disposed to look upon Cheyne-Stokes' breathing as the origin of cardiac asthma in all cases.

Cough is a frequent symptom of myocardial insufficiency. It may be nonproductive when it may be due to pressure of an enlarged left auricle on the recurrent laryngeal nerve. It is, however, more frequently productive when it may be due to several associated conditions as edema of the lungs, stasis bronchitis, bronchopneumonia, or pulmonary infarction. The character of the sputum will vary according to the associated condition. In edema of the lungs there is a large quantity of frothy serous sputum which may be tinged with bright red blood; in bronchitis and bronchopneumonia it may be mucoid or mucopurulent; in mitral disease it is frequently hemorrhagic, when it is due to capillary rupture and the patient frequently experiences a sense of relief; in pulmonary infarct it is dark red, prune-juice in character, and the symptoms, instead of being relieved, are frequently exaggerated.

Under normal conditions no notice is taken of the heart's action, but under a variety of abnormal conditions this is forced upon the consciousness of the patient, and is usually spoken of as palpitation. This frequently occurs independently of myocardial insufficiency, but is often associated with various forms of arrhythmia as with premature contractions, auricular fibrillation and the nodal rhythm associated with paroxysmal tachycardia.

Severe pain is not a prominent feature of decompensation. Sir Clifford Allbutt has pointed out that the term "anginal" has been rather loosely used in recent medical literature. The character of the pain in decompensation is rarely that of true angina pectoris. It is not severe or paroxysmal, is not attended by the peculiar dread of angina and the radiation is usually absent or little characteristic. It is rather submammary in location and of a dull aching character like the "heart ache of melancholia" and may be regarded as "a remonstrance of an overworked, engorged, inflamed, underfed, or decaying organ." It may be associated with hyperesthesia in the mammary region and with tenderness of the left sternocleidomastoid and trapezius. It rarely may assume a true anginal character in association with mitral stenosis, sudden embolism and pericarditis.

Cyanosis, a bluish or deep purple discoloration of the acral parts of the body and mucous membranes, is not infrequently present. It is due to the marked reduction of oxyhemoglobin to hemoglobin which is favored by venous obstruction which produces slowing of the blood stream and dilation of the superficial vessels.

Icterus is not uncommon. It may be due to catarrh of the bile ducts, hepatic congestion, or to gall-stones which are not infrequently associated with cardiac disease.

The edema of myocardial insufficiency has several characteristics which differentiate it particularly from the edema of nephrosis. It tends to occur first in the most dependent parts of the body. When the patient is up and about it appears first in the lower extremities; when recumbent, on the posterior surfaces of the body; or if the patient lie long on one side, the lower arm may be more edematous. While in severe cardiac decompensation most of the subcutaneous tissues of the body may take part in the edema, the scalp is rarely involved in cardiac edema. The serous cavities quite frequently contain fluid. Ascites from back pressure may be great. Effusion into both pleural cavities may occur, although the right is more apt to contain fluid in greater quantity when it is present in both sides. The hydrothorax of nephrosis is more likely to be bilateral. The increased tendency to right hydrothorax in cardiac disease was formerly explained by pressure of the dilated right heart on the root of the right lung indirectly pinching the major azygos vein as it curves over the root of the right lung to enter the superior vena cava. Fetterolf and Landis, however, present good evidence to show that the effusion comes from the visceral layer of the pleura and that it is due to the pressure of the dilated auricles on the pulmonary veins. The greater frequency in the right side is due to the fact that the dilatation of the right auricle is more common and more easy than a similar condition of the left side. No satisfactory explanation has been offered for the vagaries of cardiac edema—why it occurs in some cases and not in others or why it may sometimes be present in the serous cavities and absent in the subcutaneous tissues. The edema fluid of cardiac origin does not present the pseudochylous appearance of the edema of nephrosis. In cardiac edema the total protein content is greater; the ratio of albumin to globulin and the percentage of globulin in protein are much less. While the mechanical factors such as increased pressure in the veins and capillaries, slowing of the blood stream, and the interference with the lymph flow play an important part in the production of the edema of heart disease, it would appear that injury of the vessel wall from toxic, vasomotor, bacterial, or metabolic influence is also necessary. An hydremic condition of the blood may be an additional factor. As a result of chronic passive congestion, there is an overfilling of the blood-vessels of the alimentary tract and consequent impairment of the organs of digestion. Anorexia and indigestion result and, in marked failure of the right side of the heart, may be extreme.

The chemism and motility of the stomach are impaired, and as a result the food undergoes fermentation with the production of flatulence, which further embarrasses the heart's action.

Vomiting may be extreme in the late stages of decompensation. Its mechanism is not clear. It is usually associated with left-sided heart failure and may be attributed to deficiency of blood supply to the medulla and a stimulation of the vomiting center. It may, however, be the result of reflex stimulation of the vomiting center by means of afferent impulses from the stomach through the vagus.

By the same mechanism, meteorism arises in the intestines, and the decreased secretory activity and the diminished motility produce constipation which is often present. On the other hand, the edema may be great and the irritation so marked that diarrhea may result.

Hemorrhoids are frequently present as a result of portal obstruction.

Pain in the abdomen not infrequently occurs in myocardial insufficiency. It varies in character and mechanism. A dull aching pain in the epigastrium increased by pressure and the ingestion of food is often present as a result of the swollen congested liver. More severe pain may be caused by embolism of the spleen or intestines.

Psychical symptoms are common in cardiac decompensation. Insomnia, mania, and unconsciousness as a result of insufficient blood reaching the brain may occur. Stupor and drowsiness are less common.

PHYSICAL FINDINGS.—In relative myocardial insufficiency, the physical findings will depend upon the causative disease. Most frequently there will be hypertrophy of the left ventricle with beginning dilation. One of the first signs of failure of the left ventricle will be the presence of râles over the bases of the lungs posteriorly. If the ventricle becomes much dilated there will be the signs of relative mitral insufficiency. The rhythm of the pulse before failure of the right ventricle is remarkably good, though extrasystoles may be present. In cases dependent upon renal hypertension, presystolic gallop rhythm is quite common.

In complete decompensation the heart is dilated as shown by the diffuse wavy apex beat, the widening of the area of cardiac dulness to the left and right, blurring and softening of the heart sounds, blowing murmurs of relative mitral insufficiency, and less commonly of tricuspid insufficiency. Now marked disturbance of rhythm appear, premature contractions, auricular fibrillation, pulsus alternans, tachycardia. Pulse deficit is also often present. There is engorgement of the veins of the neck and a systolic venous pulse may be made out. Over the bases of the lungs, there is impaired resonance, diminished breath sounds and crackling râles as well as frequently signs of fluid in the pleural cavities. Areas of consolidation, over which there is a pleuritic friction rub with the characteristic sputum, indicate hemorrhagic infarction. In the abdomen, the liver will be found enlarged and tender, and frequently pulsation of same can be made out. The spleen may be palpable and the signs of free fluid in the abdominal cavity are often present.

The symptoms and signs of obstruction of the inferior vena cava will depend upon the cause of the obstruction, such as chronic mediastinitis, mediastinal tumor, increased intra-abdominal tension as by ascites or large tumor, pressure from without, without markedly increased intra-abdominal tension as by malignant tumors of the retroperitoneal lymph spaces and by thrombosis of the inferior vena cava. Marked distention of the abdominal veins with reversed blood flow is significant.

THE URINE.—In relative myocardial insufficiency there are remarkably few changes from normal in the urine. The patient will frequently complain of nycturia and there may be a night polyuria which should not be confused with the nycturic polyuria of nephritis. That of cardiac origin will usually be associated with a day oliguria. In complete cardiac decompensation, the quantity of urine is diminished in amount; it is dark in color and shows a heavy precipitate of urates; albumin is present in varying quantity; and in the sediment there are, besides the urates and uric acid crystals, casts which may be of all kinds, and a few red and white blood-cells.

KIDNEY FUNCTION.—That the kidney function is impaired in chronic passive congestion of the kidney may be shown both clinically and experimentally. The impairment varies according to the condition, *i.e.*, according to the stage of the decompensation or whether the chronic passive congestion is superimposed on a nephritis.

The response to the Mosenthal kidney test-meal in long-standing relative myocardial insufficiency and in the stage of edema of complete decompensation shows the following:

"(1) A fixed specific gravity at about 1020 in the day urine.

"(2) Diminished output of salt. The low percentage of figures for salt are outspoken.

"(3) An adequate nitrogen output. The very high concentration of nitrogen is in marked contrast to that of salt.

"(4) An oliguria.

"(5) A normal night urine."[1]

During the stage of the elimination of edema there will be the following:

"(1) A low and somewhat fixed specific gravity.

"(2) Nitrogen elimination normal.

"(3) The salt and water excretion exceed the amount ingested.

"(4) The night urine is increased and has a low percentage of nitrogen."

After the elimination of edema, the following results may be obtained:

"(1) A low moderately fixed specific gravity.

"(2) Normal nitrogen and water output.

"(3) Slightly diminished salt excretion.

"(4) The night urine may or may not be increased in quantity; its specific gravity and nitrogen concentration are low."

In myocardial insufficiency associated with chronic nephritis the results may exhibit the characteristics of either lesion; usually, however, the chronic passive congestion proves itself the predominating feature (Mosenthal). The phenolsulphonephthalein output may be markedly lowered in pure chronic passive congestion or that associated with nephritis. When low renal function is followed by an increased phthalein output, the amount of increase gives a fair approximation of the extent of cardiac decompensation. In pure passive congestion the non-protein nitrogen very rarely shows an increase above 50 mg. per 100 c.c. of blood. A phthalein rapidly returning to normal, associated with a low level of blood urea, speaks strongly for passive congestion as the underlying factor.

In pure passive congestion, Ambard's coefficient is rarely above .15. This rapidly falls to normal with return of compensation (Rowntree).

The diagnosis of pure passive congestion and that associated with nephritis may be made by a consideration of what has been stated with reference to the clinical history, physical findings, and functional conditions which need not be repeated.

Treatment.—The indications for treatment are offered by the underlying cause. This is usually the myocardial insufficiency and the measures to be carried out are much the same whatever may be the cause of this. **Rest,** absolute in bed when possible, should be insisted upon. If the dyspnea is great, the patient may be more comfortable on a **back rest,** or in the severest cases the position most comfortable to the patient may be allowed. The rest should be continued until the serious manifestations disappear. In the chronic cases and those with partial decompensation, the patient may be allowed to be wheeled in a chair into the open. The **diet** requires careful supervision. The quantity of food in the meal and the number of meals should be given attention. It is much better to order small amounts of food in five feedings per day than larger meals three times a day. The salt and fluid intake must be markedly restricted. In severe cases of myocardial insufficiency the **Karell diet** is attended by its most brilliant results. This consists of 200 c.c. of milk four times a day and nothing else. After four or five days, or in less severe cases, the author has found Rowntree's modification of this diet excellent:

9 A. M.—200 c.c. of milk (1/3 pint).
1 shredded wheat biscuit.
1 egg, soft boiled or poached.
1 slice of bread, salt free.
1 butter ball, salt free.
1 P. M.—Soup (chicken or tomato), 200 c.c., no salt.
Lamb chop, 100 grams (.3 lb.), or chicken 150 grams (.4 lb.).
Mashed potatoes, 100 grams (.3 lb.).
1 soda cracker, salt free.
5 P. M.—Milk, 200 c.c.
1 egg, soft boiled or poached.
1 slice of bread, 40 grams, salt free.
Rice, or tapioca pudding, 100 grams (.3 lb.).
9 P. M.—Milk, 200 c.c.
1 A. M.—Milk, 200 c.c.
5 A. M.—Milk, 200 c.c.

The fluids should be restricted according to the amount of edema present. At first the total quantity should rarely exceed 1000 or 1500 c.c. It is practically impossible to arrange a salt-free diet; in severe cases where the salt concentration in the urine is low, no salt at all should be added. With improvement in the salt concentration, the salt may be carefully added. It is surprising how rapidly the edema disappears and the heart improves under these measures. Other methods, such as depletion, support of the heart, diuretics, and symptomatic treatment must not be neglected and frequently will be necessary. In acute dilation of the right heart with severe orthopnea, **venesection** may be necessary even in the presence of anemia. The quantity of blood withdrawn will depend upon the condition present. If the hemoglobin percentage is not very low, below 70 per cent., 400 to 600 c.c. should be removed; if lower it will probably be better to remove smaller quantities. If the patient has not previously had **digitalis, amorphous strophanthin,** grain 1/200 (.00032 gram), or better, **ouabain,** in one-half the dose, may be administered intramuscularly. The local disagreeable effects may be overcome by local massage for fifteen minutes. If the accumulation of fluid in the serous cavities produces disagreeable effects, it should be removed by **paracentesis.** It is also desirable to secure free bowel movements. **Magnesium sulphate,** ½ ounce (16 grams), one or two **compound cathartic pills, compound jalap powder,** grains 30 (1.95 grams), or **eletarin,** grain 1/20 to 1/10 (.00324 to .00648 gram) may be given. It is the author's belief that in complete cardiac decompensation, whatever the cause—whether the heart is rapid and fibrillating, or the rhythm is normal, or whether chronic diffuse glomerulonephritis, benign hypertension or the combination form is present—digitalis is indicated. The essentials in its administration are the knowledge of an active preparation, the symptoms of its toxic effect, and the pushing it to its therapeutic effect. Given standardized leaves, the tincture or infusion in doses equivalent to grains 1½ (.0974 gram) of the leaves may be given every four hours, for forty-eight hours. The author prefers **digipuratum**, now known as **digitan**, the tablets of which represent 1½ grains (1.0974 gram) of the standardized leaves. If the desired diuresis does not result, the **caffein diuretics** will be valuable aids. These are best administered according to the method of Romberg's clinic—**caffein citrate**, grains 2 (.13 gram), **diuretin**, grains 10 (.65 gram), or **theocin**, grains 3 (.195 gram), may be given and repeated for three doses. These should not be repeated until their diuretic effect begins to subside. A diminishing quantity of urine, the occurrence of a pulse of 60, an abnormal rhythm, especially a bigeminal pulse, or nausea, vomiting, or headache are the indications for stopping the digitalis. The continuance of this drug in the so-called chronic digitalis treatment will depend upon the character of the case.

SYMPTOMATIC TREATMENT.—The edema will be controlled, if at all, by rest, restriction of fluids and salt, paracentesis, digitalis, and the caffein derivatives as described above.

For the dyspnea, it will be desirable to determine the cause and remove it if possible, control flatulence by proper attention to the diet, the use of the back rest, the administration of **morphin** and **atropin**, and venesection followed by strophanthin may be necessary.

Palpitation and cardiac distress may usually be overcome by attention to the gastro-intestinal tract and the application of the **ice-bag** or **small blisters over the precordium.**

The gastric symptoms may be the result of digitalis or purgatives and if so, these should be withdrawn as well as all food for twelve hours and gastric sedatives given internally with the application of counter-irritants over the epigastrium.

Cough will usually respond to the general measures described above without the necessity of expectorant mixtures.

Hemoptysis may occur and requires insistence on absolute quiet and the use of the ice-bag.

Edema of the lungs occurring acutely and severely may sometimes be relieved by morphin, but sometimes venesection combined with morphin will be life-saving in this condition.

Insomnia will often require the back rest and the administration of sedatives and hypnotics.

Pathology.—Macroscopically the kidney will usually be found somewhat enlarged, of an extreme rubbery consistency, and of a deep purplish gray color. The surface is smooth and the capsule is not adherent; on cut section, the color is gray purplish and striations are quite distinct. In the cortex, the glomeruli and blood-vessels show red and the tubules gray. The pyramids are deeply reddened.

Microscopically the glomerular loops are distended with blood. Coagulated fluid may be found in the capsular space and casts in the tubules. The tubular epithelium may show cloudy swelling. The interstitial connective tissue may be increased, but usually is not much in evidence, the hardness being due to the distention with blood.

THE FOCAL ATHEROSCLEROTIC KIDNEY

(*Senile Arteriosclerotic Kidney, Decrescent Arteriosclerotic Kidney*)

Symptomatology.—CLINICAL HISTORY.—The symptoms of focal atherosclerotic kidney are those of senile or decrescent arteriosclerosis in which it occurs as a part of the general process. They are usually gradual in onset, and, as expressed by Sir T. Clifford Allbutt, are for the greater part negative and consist in a drought of the body, in failing irrigation of the organs such as the cardiac, the renal, the cerebrospinal, the gastro-intestinal, and the rest. The withered skin, the shrunken limbs and the shuffling gait may be noted, or the onset may be more rapid, the result of premature old age, and the symptoms may be those of progressive cachexia with pallor and emaciation.

The blood-pressure is not increased, rarely transitory rises may be noted, and the heart is not hypertrophied. The symptoms which will be found to form such a prominent part of the clinical history of benign hypertension are conspicuous by their absence.

Dyspnea may be present as a result of emphysema which so frequently occurs in this condition. There may be anorexia, loss of flesh, hypochlorhydria or achlorhydria which, with hematemesis sometimes occurring as a result of local atrophy dependent upon atherosclerosis of the gastric vessels, awaken the thought of carcinoma of the stomach. From the same lesions in the intestinal vessels, flatulence, melena, and other intestinal symptoms may be present. Sclerosis of the pancreatic vessels may be attended with markedly fatty stools and a trace of sugar in the urine. Severe abdominal pain from spasm and cramp in the intra-abdominal vessels is not a feature of senile arteriosclerosis.

The cerebral palsies of decrescent arteriosclerosis are atrophic rather than hemorrhagic in nature. They result from a lacunar process, irregular cavities being formed by areas of atrophic softening, or from thromboses, the formation of which are favored by the arteriosclerotic cerebral vessels. Rarely, hemiplegia from cerebral hemorrhage may occur as the result of the transitory hypertension which sometimes comes on in these cases. Severe and profound melancholia, associated not only with obsessions but delusions, may occur. Garrulity, tearfulness, loss of memory, disorders of sleep, especially insomnia in the early morning, are familiar symptoms of senile arteriosclerosis.

The eye-grounds may show changes which are more likely to depend upon degeneration due mainly to deficient nutrition than to edema.

PHYSICAL FINDINGS.—The general appearance has already been referred to. The visible and palpable arteries will usually show marked arteriosclerotic changes. The beaded, tortuous arteries are much more frequent in this condition than in benign hypertension. The heart does not show evidence of hypertrophy, though a systolic murmur at the apex may be present as the result of atherosclerotic processes in the mitral valve. There may be hyperresonance with prolonged expiratory sound as the result of emphysma. The reflexes may be increased.

Laboratory Findings.—The urine shows slight or no abnormal changes—a trace of albumin, a few hyalin casts and red blood-cells may be found in the centrifuged specimen. The blood often shows a mild secondary anemia.

The functional capacity of the kidneys is very little affected in the senile arteriosclerotic kidney. The results of the concentration tests, the phenolsulphonephthalein excretion, and the figures for non-protein nitrogen and urea in the blood are within normal limits.

Treatment.—As Sir T. Clifford Allbutt says, "Decrescent arteriosclerosis is **immedicable.** We cannot hold time by the wings, and with some men it flies faster than with others." The mild degrees of increased pressure which belongs to advanced age should not be interfered with. Those cases showing marked transitory rises of pressure should receive the treatment of benign hypertension. The quality of the blood may be improved by mild alteratives, mild baths, moderate exercise short of fatigue in the open, by careful attention to the excretory organs, and by **ferruginous tonics.**

Pathology.—The kidneys may be normal, slightly enlarged, or slightly reduced in size. They are firmer than normal. There may, in various areas on the surface of the kidney, be depressions corresponding to localized or patchy atrophy due to arteriosclerosis of vessels supplying the part. These usually produce rather large areas of unevenness since here it is the larger vessels which are involved in the atherosclerotic process. On microscopical examination there will be found the evidences of atherosclerosis of the larger vessels with atrophy of the areas supplied by these while the other portions of the parenchyma will be found intact.

THE NEPHROPATHIES GENERALLY INCLUDED UNDER THE GENETIC TERM BRIGHT'S DISEASE

Introduction.—The term, Bright's disease, in its original significance included diseases of the kidney associated with albuminuria and dropsy. To-day it is used in a much broader sense and includes a variety of degenerative, inflammatory, and atherosclerotic processes in the kidney to which the term nephritis has been applied clinically. These conditions have usually been described in text-books under the heads of acute parenchymatous nephritis, chronic parenchymatous nephritis, and chronic interstitial nephritis. It has been difficult to arrive at a classification of these nephropathies equally satisfactory to the clinician and the pathological anatomist because there has been no harmony as to the pathogenesis of the various forms.

On the pathological side, it has been questioned whether there is such a thing as parenchymatous inflammation as applied to the kidney. Lubarsch states that it is impossible to differentiate whether there is a progressive or a regressive process in a cell in the stage of cloudy swelling; further, that if one holds that inflammation must always be a progressive process, one must discard the idea of a parenchymatous inflammation. Ribbert holds that the epithelium does not inflame and that all regressive processes must be excluded from the picture of inflammation. He further holds that inflammation is an accompaniment and not the fundamental cause of the disease process, that the disease-producing process is always found in the regressive parenchymatous changes to which the inflammation is secondary. Ribbert thus accepts the view of Weigert that every inflammation is produced by a parenchymatous lesion; he would speak only of acute, subacute, and chronic nephritis and reserve the name nephrosis for those lesions which are only of a degenerative nature. Löhlein has, however, shown that a large number of cases which were earlier designated as chronic parenchymatous nephritis arises from chronic glomerulonephritis, therefore from cases in which the parenchymatous degeneration did not precede the inflammatory changes in the glomeruli, but in a great measure was produced by them. On the other hand, Aschoff holds to the view of a parenchymatous inflammation, emphasizing the nature of the inflammatory process as a reaction to an injury, which as Adami states is adaptive in character. Aschoff emphasizes that up to cell death there are all possible transitions, that, in any case, a stage precedes cell death in which the cell is swollen, excretion increased, therefore showing active manifestations of life. In acute hematogenous diseases of the kidney, Aschoff differentiates degenerations, dependent upon disturbances of metabolism (amyloid, system necroses in poisoning), and those which show changes based on circulatory disturbances—inflammation with predominating reactions in the vascular connective tissue (nephritis exudativa serosa, nephritis exudativa purulenta, nephritis interstitialis acuta), and inflammation with predominating reaction in the filtration and secretory apparatus, nephritis tubularis (parenchymatous inflammation), glomerulonephritis, and a mixed form of tubular and glomerular nephritis.

Volhard, using increased blood-pressure as the clinical indication of the presence of an acute, subacute, or chronic nephritis, found that the old clinical syndrome expressed by the term chronic parenchymatous nephritis included two groups of cases which differentiated themselves by the condition of the blood-pressure. In the group without increased blood-pressure, there was found at autopsy, macroscopically, the large white kidney. Yet microscopical examination of these kidneys failed to show any evidence of inflammatory changes—hyperemia, stasis, exudation, proliferation—but evidence of certain forms of degeneration of the epithelium of the kidney tubules; while in the group with increased blood-pressure, these evidences of inflammation were present in the glomeruli. Fahr, however, has shown that later in these cases there may be evidence of a secondary inflammatory process in the interstitial tissue, that indeed, in the final stage of these kidneys a markedly contracted kidney may occur as the result of replacement fibrosis without manifestations of inflammation in the glomeruli.

In the course of further clinical and anatomical investigation, it was found that true inflammatory processes may occur in the kidney with the absence of increased blood-pressure. These cases included a group of hemorrhagic focal nephritides, such as the embolic focal nephritis of Löhlein, occurring chiefly in streptococcic viridans sepsis, the acute interstitial focal nephritis described by Reichel and Councilman, as occurring after scarlet fever and septic processes, and the focal glomerulonephritis which also occurs in septic processes like scarlet fever, angina, etc.

It was also found that the so-called interstitial indurative nephritis did not represent a single entity. The work of Jores, Fahr, Gaskell, and others, has shown that these kidneys are not the outcome of a gradual interstitial inflammation, but that they are primarily due to arteriosclerosis of the small and smallest blood-vessels of the kidney. This group is characterized by high blood-pressure and cardiac hypertrophy, but the condition of the kidney function served to show that here are two subgroups: the one without disturbance of kidney function which Volhard and Fahr designate as benign hypertension, which Janeway called hypertensive cardiovascular disease, and which Clifford Allbutt speaks of as hyperpiesis; the other with disturbance of kidney function designated by Volhard and Fahr as malignant hypertension, the combination form—arteriosclerosis plus nephritis.

It therefore appears that the old terms, parenchymatous and interstitial, with which there has been painful disagreement between the clinical and anatomical diagnoses, had best be discarded, and the classification of these nephropathies approached from the clinical, functional and anatomical standpoints, which offers advantages for diagnosis, prognosis and treatment. The classification of Volhard and Fahr, which the work of other observers has tended to confirm, seems best. They with F. von Müller designate the degenerative nephropathies as nephroses, the inflammatory as nephritides, and the arteriosclerotic processes as scleroses, and suggest the following classification:

A. Degeneration diseases: *Nephroses*, genuine and of known etiology, with and without amyloid degeneration of the vessels.
  (1) Acute course.
  (2) Chronic course.
  (3) End stage: Nephrotic contracted kidney without increased blood-pressure.
B. Inflammatory diseases: *Nephritides.*
  (1) Diffuse glomerulonephritis with obligatory increased blood-pressure, course in three stages:
    (*a*) Acute stage
    (*b*) Chronic stage without kidney insufficiency.
    (*c*) End stage, with kidney insufficiency.
    All three stages may run a course
      (*a*) Without edema.
      (*b*) With edema, *i.e.*, with marked and diffuse degeneration of the epithelium.
  (2) Focal nephritis, without increased blood-pressure.
    (*a*) Focal glomerulonephritis.
      1. Acute stage.
      2. Chronic stage.
    (*b*) Septic interstitial nephritis.
    (*c*) Embolic focal nephritis.
C. Arteriosclerotic diseases: *Scleroses.*
  (1) Benign hypertension—pure sclerosis of the kidney vessels.
  (2) Malignant hypertension—the combination form, genuine contracted kidney—sclerosis plus nephritis.

NEPHROSIS

(*Degenerative Nephropathy, Parenchymatous Nephritis, Tubular Nephritis.*)

Definition.—Under the term nephrosis, the pathologist includes all degenerative lesions (cloudy swelling, granular and fatty degeneration, and necrosis) of the kidney in which the inflammatory lesions are not above suspicion. Cloudy swelling, designated pathologically as the first stage of nephrosis, gives rise to no symptoms other than albuminuria and cylindruria, while necrotic lesions give rise to a special symptomatology which will be described under necrotizing nephrosis as represented by the sublimate kidney.

The clinical picture to be described includes the forms heretofore known as chronic parenchymatous nephritis without increased blood-pressure, and represented by kidneys showing granular degeneration and fatty degeneration of the epithelium of the tubules without inflammatory changes in the glomeruli.

Etiology.—The nephroses occur much less frequently than other nephropathies. Volhard and Fahr had 55 cases among 565 cases of Bright's disease. The author saw 10 cases in about 100 cases of the nephropathies. The degenerative lesions of the kidney may be divided into two groups with respect to etiology. In the first group, which includes the purest and most typical cases, no cause can be discovered. These have been called genuine nephrosis. There is, however, some evidence to show that exposure to cold and heredity may play a slight rôle as predisposing causes. Recent experimental work would also indicate that a continued high protein diet may produce degenerative lesions of the kidneys in rabbits which are similar to those found in the kidney in human cases of nephrosis. Newburgh states with reference to these lesions that "the lesion is not the result of arteriosclerosis, for the arteries are not diseased. Nor are we dealing with a primary glomerulonephritis. Judging by the constancy and severity of the damage to the epithelium of the convoluted tubules, the firm impression is gained that the offending substance has the primary and chief deleterious effect upon these and the slowly progressing injury of the proximal convoluted tubules is accompanied by an overgrowth of connective tissue." While Newburgh does not claim this for his sections, the author thinks they are strikingly like those described and pictured by Fahr for the various stages of nephrosis, *i.e.*, from cloudy swelling through the stage of demonstrable lesions in the epithelium and inflammatory reaction in the connective tissue to the end stage of nephrotic contracted kidney.

In the second group, which are more frequent, are those cases which are the result of known causes. These are the toxins of infectious agents, endogenous toxins and the toxic action of various metals.

INFECTIOUS AGENTS.—Why the toxins of bacteria when acting on the kidney will at one time excite an inflammatory reaction in the glomeruli, at another time produce degenerative lesions in the epithelium chiefly of the proximal convoluted tubules, or occasionally both of these lesions together, is not understood. It can scarcely be due to the difference in reaction in the vascular connective tissue and the epithelium, because there are pure cases of nephrosis and diffuse glomerulonephritis which are the result of the same cause. It has been suggested that the degenerative lesion may be the result of the specific infection and the nephritis due to a complicating streptococcus infection. Some observers have claimed that the injection of tuberculin may cause a glomerulonephritis, and it is suggested that in this instance the nephritis may be due to the tuberculin and the nephrosis due to the toxins resulting from the disintegration of tissue cells, which latter may be a factor in the production of nephrosis in other infections.

Nephrosis, according to Volhard and Fahr's experience, is most frequently associated with *tuberculosis,* especially tuberculosis of the lymph glands and bones. Fifteen of their 55 cases were ascribed to tuberculosis. In one of the author's 10 cases pulmonary tuberculosis was the only apparent cause. Munk has emphasized the importance of *syphilis* as a cause of degenerative lesions in the kidney. Volhard and Fahr had 7 cases due to syphilis among 55 cases. In 4 of the author's 10 cases syphilis was the apparent cause. *Chronic suppurative processes* are also responsible for some cases of nephrosis. All of these causes, tuberculosis, syphilis, and chronic suppurative processes, are usually regarded as giving rise to amyloid disease of the kidney, and the most of the kidney diseases resulting from these causes have been regarded as amyloid disease. But, as we shall see, the same symptoms occur with the nephroses whether they are accompanied by the deposit of amyloid substance in the kidney or not, so that the presence of amyloid is a complication which often can be diagnosed only at autopsy.

Nephrosis may rarely occur in the course of other infectious diseases, such as diphtheria, typhoid fever, measles, cholera, and yellow fever. The hemoglobinuric kidney most frequently shows a degenerative lesion of the epithelium with slight or no involvement of the glomeruli. Yet the symptoms of hemoglobinuric fever rarely correspond to that of the second stage of nephrosis. The edema is usually lacking and there is frequently an increase of blood-pressure. We may have here a condition analogous to that of severe mercurial poisoning in which there is absence of edema and the presence of increased blood-pressure with marked nitrogen retention in the blood. The increased blood-pressure in both may be due to the anuria and increase of non-protein nitrogen in the blood.

ENDOGENOUS TOXINS.—The *kidney of pregnancy* which arises as the result of an intoxication of the body by the passage into the maternal circulation of ferments and autolytic products from the placenta is frequently a purely degenerative lesion of tubular epithelium. It is true that this kidney of pregnancy is also often superimposed upon an old nephritis which has existed a long time before the pregnancy; an acute nephritis may develop along with the nephrosis of pregnancy when in either case the clinical history and findings may indicate the association of the two conditions. It is also possible that some of these cases may show increased blood-pressure and changes in the eye-grounds without inflammatory changes in the glomeruli which are at variance with the clinical history of a pure nephrosis. In such cases there may be marked vascular changes, and it is possible that these as well as the increased blood-pressure are due to the placental toxins.

Cachectic conditions which occur as the result of malignant tumors may give rise to nephrosis.

Metallic poisons may give rise to purely degenerative lesions of the kidney. Of these phosphorus, bichromate of potash and bichlorid of mercury may be mentioned. The latter is the most important from a clinical standpoint.

The table taken from Volhard and Fahr with the author's cases included will illustrate not only the etiology of nephrosis, but also the causes of the different stages of the disease.

After Volhard and Fahr with Author's Cases Added

Type	Acute	Chronic	End Stage	Total
Genuine		7 + 1 = 8		
Pregnancy	2			
Diphtheria	7			
Tuberculosis		15 + 1 = 16	3	
Lues	2 + 1 = 3	5 + 3 = 8		
Chronic Suppurative		3		
Pancarditis (Viridans sepsis)		2		
Staphylococcic sepsis	1			
Measles	1			
Sarcomatosis		1		
Bichlorid of mercury	6 + 4 = 10			
Total	24	38	3	65

Symptomatology.—There is no period of incubation as is apparent in some cases of diffuse glomerulonephritis. The onset is gradual and insidious. The patient is rarely able to state definitely the time of beginning. The symptoms which usually take the patient to the physician are anorexia, fatigability, pallor of the skin, matutinal edema of the eyelids and edema of the feet, when upon examination a high albuminuria will be present. The skin presents a clear bluish-white color in marked contrast to the blood findings unless anemia is present as a result of the causative disease. Anorexia is present during the stage of the edema, but the appetite may later be but little impaired, even voracious. There is a marked tendency to diarrhea which may be profuse and painless especially during the edematous stage, and is probably due to the increased permeability of the blood-vessels of the intestinal tract. A marked feature is the absence of increased blood-pressure and cardiac hypertrophy except in those cases in which arteriosclerosis existed before the onset. As a rule there are no abnormal changes in the eye-grounds.

In the beginning the subjective symptoms are not prominent. The patient may complain of fatigue, weakness and emaciation which is at first obscured by the edema. The long continuance of the disease with pitiful sameness renders the patient altogether miserable.

PHYSICAL FINDINGS.—On physical examination edema is apparent and dominates the clinical picture of the disease. It usually begins in the face and rapidly involves the subcutaneous tissues of the whole body, the external genitals and the serous cavities. Hydrothorax and ascites may be present without the generalized edema.

The edema fluid is characterized by a milky, cloudy, pseudochylous appearance, probably due to globulin-lipoid substances. The blood-serum shows the same appearance, which probably arises from the fatty kidneys, since the same double refracting lipoid substance is present in the interstitial tissue and endothelium of lymph vessels of such kidneys. The fluid is watery and poor in proteins, the albumin content, according to the Esbach test, being from .25 to .5 per cent. The nitrogen content, according to Volhard and Fahr, is from .036 to .12 per cent. and the sodium chlorid concentration the same as that in the blood, from .62 to .7 per cent. The specific gravity does not usually exceed 1010. Epstein has made some interesting studies upon these edema fluids. He states that these fluids are unlike those present in any other condition and are composed almost exclusively of inorganic and nitrogenous salts and water, but that they differ somewhat according to whether they are cutaneous, pleural or abdominal effusions. The cutaneous effusions are characterized by a very low protein content, a small amount of noncoagulable nitrogen, a relatively very large quantity of globulin, and the chlorids in about the same proportion as in the blood-serum. The pleural effusions differ from the cutaneous by their higher protein content. In them, the incoagulable nitrogen is uniformly low, and the chlorids vary in amount according to the case. The abdominal fluids in general are less rich in protein than pleural effusions.

There has been and still is much discussion as to the cause of edema occurring in kidney diseases. On the experimental side, it has pretty generally been found that there must be three factors present for the production of edema, *viz.*, glomerular lesion, vascular lesion, and hydremia (Pearce). According to Widal the edema is a result of a failure on the part of the kidney to excrete salt and water. Fischer believes that the cause of edema is to be found in the tissue, and that it is due to an increased affinity of the colloids of the tissues for water and this in turn is due to the accumulation of acids in the tissues. Volhard and Fahr state that the cause of the edema is to be sought in a pathologically increased permeability of the blood-vessels, and this apparently arises under the influence of substances which originate from the degeneration of the kidney epithelium and is carried into the circulation. They state further that in the stage of most marked edema there is no hydremia, and that the viscosity of the blood may be increased, which they think shows that the edema does not depend upon a water retention, the result of insufficient excretion of water, but on the contrary that the poor water excretion is apparently the result of a lack of water in the blood.

Epstein, as a result of a study of the blood-serum and edema fluids in these cases, offers a similar view. He states that the loss of protein incurred by the blood-serum through the continuous albuminuria causes a decrease in the osmotic pressure of the blood. Through this condition, and the additional circumstance that large quantities of fats and lipoids accumulate therein, the physicochemical state of the blood is disturbed to such an extent that it loses much of the power which it normally possesses to withdraw fluids from the tissues; consequently deposition of fluid in the tissues occurs. In other words, the edema in this type of nephritis is not necessarily the result of lessened permeability or functional powers of the kidneys to eliminate salt and water, but is the result of a change in the character of the blood.

In the chest there will frequently be found the physical signs of fluid in both pleural cavities. The heart does not show any evidence of hypertrophy which with the normal blood-pressure forms one of the chief characteristics of the disease. In the abdomen may be found the signs of the presence of free fluid.

Blood.—Unless anemia is present as a result of the causative disease, the red blood-cells are not diminished. A case dependent upon syphilis showed red blood-cells 5,182,000, leukocytes 9,000, polymorphonuclears 66 per cent., small lymphocytes 31 per cent., large mononuclears 0, eosinophils 3 per cent., Wassermann positive. There are conflicting views with respect to hydremia. Volhard and Fahr state that there is no hydremia at the time of most marked edema, that on the contrary the blood is abnormally concentrated. They state further that the term hydremia is confusing, that the assumption of an actual blood thinning is only justifiable when the number of red blood-cells is diminished in the thin suspension, that one is not justified in concluding that a hydremia is present from the decrease in the protein content. This, however, is not in accord with the usual views as to hydremia. Hewlett states that hydremia means a watery condition of the blood, and that since the corpuscular elements of the blood are relatively rich in solids, their number markedly influences the percentage of water in the total blood. He states, however, that it seems advisable to exclude from consideration the changes of the blood concentration which are caused by variation in the number of corpuscles, and thus restricted, the term hydremia means a watery condition of the blood-serum or blood-plasma. Epstein's examination in two cases of nephrosis shows the following:

Per 100 c.c.

Total Protein (Gram)	Incoagulable Nitrogen (Gram)	Globulin (Gram)	Chlorid (Gram)	Cholesterol (Gram)	Globulin in Protein (Per Cent.)
3.611	0.063	2.038	0.404	0.760	59
2.731	0.101	2.598	0.390	1.226	95

Urine.—The quantity of urine in the stage of the formation and maintenance of edema is markedly diminished. Less than 500 c.c.

in twenty-four hours is not infrequent. During the stage of elimination of edema the quantity is increased. It varies in color from a grayish yellow to a dark brown and shows a heavy precipitate of urates. With oliguria the specific gravity is high, varying from 1025 to 1050. With the increase of quantity it may be very low. The reaction is usually acid, but on account of the ease with which decomposition occurs it may be found to be alkaline. The albumin content is high, which with the absence of macroscopical blood forms the chief characteristics of the urine in this condition. The microscopical examination of the sediment gives variable results. There may be numerous casts of all kinds, fatty epithelium and leukocytes. This is especially the case in the edematous stage. Later, casts, fatty epithelium, and leukocytes may be scant. Munk has emphasized the presence of double refracting substances as of importance in the diagnosis of nephrosis.

Functional Tests.—As a rule, it may be stated that the usual tests for the determination of kidney function show good results. Volhard and Fahr state that the water test, in which 1500 c.c. of water are taken on an empty stomach, may be poor in the stage of marked edema and oliguria, but that this is due to the increased permeability of the vessels rather than to kidney insufficiency. The same obtains with reference to the salt excretion. On the contrary, the nitrogen output in the urine is increased due to the increased nitrogen concentration. According to these authors the methods of Schlayer have given paradoxical results. In one case the author has obtained the following results:

Mosenthal Test-meal

Time of Day	Quantity	Specific Gravity	NaCl		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8 A. M.–10 A. M.	70 c.c.	1020				
10 A. M.–12 M.	60 c.c.	1020				
12 M. – 2 P. M.	62 c.c.	1018				
2 – 4 P. M.	72 c.c.	1020				
4 – 6 P. M.	87 c.c.	1020				
6 – 8 P. M.	74 c.c.	1020				
Total Day	425 c.c.		.1	.425	1.5	6.37
Night (8 P. M.–8 A. M.)	600 c.c.		.04	.24	1.	6.00
Total 24 hrs.	1025 c.c.			.665		12.37
Fluid intake	1760 c.c.			8.5		13.4
Difference	+ 735 c.c.			— 7.835		1.03

Weight	Period	Blood Urea per 100 c.c.	Urine				Ambard's Coefficient
			Period	24 hrs.	Urea	Urea	
57 kg.	4–6 P. M.	40 mg.	87 c.c.	1044 c.c.	18.5 c.c. (in 24 hrs.)	17.7 c.c. (in liter)	.093

water out of the tissues into the serous cavities from which it must be removed by paracentesis. In a few cases of nephrosis, the author has not found evidence of acidosis in the carbon dioxid tension of the alveolar air and the alkali reserve of the blood. Rowntree and Christian have seen the edema unquestionably increased by the application of this treatment.

Epstein, believing that conditions of nutritional disturbance are present and that the edema is associated with definite changes in the blood, suggests the following treatment:

"In the less severe cases the patients are put on a **high protein diet** (from 80 to 200 grams of proteins daily) with a **small quantity of carbohydrates** and a **total restriction of fats.** The total food value of the diet ranges between 1200 and 2400 calories. In very severe cases repeated **transfusions of blood** are resorted to simultaneously with the administration of a high-protein, fat-poor diet. At each transfusion (about 500 c.c.) an equal amount of the patient's blood is first removed. The effect of this procedure is threefold: (*a*) It ameliorates the anemia; (*b*) it increases the protein content of the blood; and (*c*) it diminishes the fat content of the serum. As is to be expected, the effects of transfusion are temporary, but they serve to initiate the desired changes in the composition of the blood-serum. The chief reliance is placed on a high protein diet. The chlorids and water are only moderately restricted."

He states that the results of this treatment carried out in 8 cases appear encouraging. Epstein further states that we possess no evidence that protein diet *per se* is deleterious to the kidneys. The later experimental work of Newburgh referred to above should be considered in this connection.

According to the author's own experience, these patients should be kept at absolute **rest in bed** until the edema subsides. The bedding and clothing should be warm to promote the action of the skin. Since there is no impairment of the kidney function as expressed by a decreased phthalein output nor any increase in the blood urea there is no indication for an especially low protein diet. Whether the salt and water retention is due to insufficiency of the kidneys for these substances, or is due to the condition of the blood and tissues, may be discussed, but the fact remains that salt and water are retained and indicate a salt-poor, water-poor diet. As a rule the institution of this diet is followed by a marked subsidence of the edema from the subcutaneous tissues as well as from the serous cavities. Where there is difficulty in getting such a diet prepared, the author has found that the **Karell diet** (200 c.c. of milk four times a day and nothing else) is followed by good results. If the edema is extreme, other dehydrating measures may be employed. In the absence of diarrhea which, however, is frequently present, **compound jalap powder,** 1 dram (3.9 grams), may be given once daily. **Sweating by the hot air bath or wet pack** will, however, usually give better results. No beneficial results have been obtained from diuretics. The author has not found multiple incisions nor the insertion of Southey's tube nècessary nor does he think they are desirable. If the accumulation of fluid in the serous cavities is so great as to interfere with the comfort of the patient, **paracentesis** should be performed and repeated as often as necessary. Due attention should be paid to the occurrence of complications such as bronchitis and pneumonia and the treatment appropriate for these conditions instituted. The occurrence of infectious peritonitis, which not infrequently develops, demands surgical interference. Careful attention should be given the patient during convalescence, his salt and water tolerance carefully determined, exposure to undue cold and wet should be avoided, and the patient urged to pay due regard to the occurrence of focal infections, for the recurrence of the symptoms of nephrosis are extremely likely to recur.

Prognosis.—The prognosis is good so far as death referable to the kidney condition is concerned. In none of Volhard and Fahr's 55 cases has death resulted from the kidney lesion, nor in the 10 cases studied by the author. The recovery from the kidney condition is dependent largely upon the causative disease. Those cases dependent upon tuberculosis and chronic suppurative diseases rarely recover, while those due to pregnancy, diphtheria and lues frequently do. The occurrence of complications also affect the prognosis. Bronchitis and pneumonia affect it seriously. One of the author's patients with pneumonia, however, completely recovered. Infectious peritonitis is almost always fatal. Cases of genuine nephrosis may eventually recover after a very prolonged course.

Pathology.—Fahr divides the nephroses pathologically into three groups, *viz.*, simple nephrosis, specially characterized nephrosis, represented by the sublimate kidney, and complicated nephrosis, represented by the amyloid kidney.

The simple nephrosis, he further subdivides into four stages histologically, *viz.*:

First Stage.—Cloudy swelling.

Second Stage.—Histologically demonstrable degenerative lesions in the epithelium.

Third Stage.—Secondary inflammatory reaction in the interstitial tissue.

Fourth Stage.—The contraction stage.

FIRST STAGE OR STAGE OF CLOUDY SWELLING.—*Macroscopical.*—The kidney is usually slightly larger than normal; the capsule strips easily, the outer surface is smooth, varying from brown to yellow in color; it is edematous; on cut surface it is of a brownish to a yellow opaque color; the surface markings are obscured.

Microscopical.—The epithelium of the proximal convoluted tubules is swollen, narrowing the lumen of the tubules. Altmann's granules are enlarged and in some areas regularly arranged and in other areas irregularly arranged. The nuclei are generally well preserved. Fatty changes may occur in the cells of Henle's loops. The epithelium of the ascending loop of Henle and the distal convoluted tubules generally are not affected; if so, not to the extent of the proximal convoluted tubules. There is exudation of albumin into Bowman's capsule and in the lumen of the tubules. The glomerular loops are well filled with blood. These changes which are quite frequent in all infectious processes usually completely recover, but may pass over into the next or second stage.

SECOND STAGE.—*Macroscopical.*—The kidney is enlarged; the capsule strips easily; the outer surface is smooth; the consistence is spongy; the cortex is widened and of a smutty color; the medulla is brown in color in marked contrast to the cortex.

Microscopical.—The chief characteristics of this stage are hyalin, granular and fatty degeneration of the epithelium of the proximal convoluted tubules. The nuclei of these cells are partly preserved and partly destroyed. There has been much discussion as to the origin and significance of these hyalin granules. Some maintain that they arise from the Altmann granules and signify a hyperfunction. The weight of opinion seems to regard these cells as the result of a degenerative process. The distal portion of the proximal convoluted tubule, which frequently has been confused with the ascending limb of Henle's loop, is chiefly affected. Fatty degeneration is also present usually in a greater degree than in the stage of cloudy swelling. This usually increases with the degree of hyalin degeneration, but the changes are not exactly parallel. The fatty changes attack chiefly the proximal convoluted tubules, though the ascending limb of Henle's loop and the distal convoluted tubule may be involved to a less extent. Occasionally casts are present in the descending limb and loop.

In the capsular space there is coagulated albumin and occasionally desquamated epithelium. The glomerular loops are well filled with blood, but there are no signs of inflammation. The capillaries of the medulla are also well filled, though there is no evidence of inflammatory reaction in the interstitial tissue. This stage also usually heals, but rarely passes over into the third stage.

THIRD STAGE.—*Macroscopical.*—The macroscopical appearance is more characteristic in this stage than in the two previous stages. The kidney is smaller than that of the second stage, but usually larger than normal. The capsule strips easily. The outer surface is smooth and smutty in appearance. There are opaque grayish spots distributed throughout the substance and the consistence is soft and doughy. On cut surface the cortex is widened in appearance similar to the outer surface, with gray spots and streaks. The markings are obscured. The medulla is brownish in color.

Microscopical.—The microscopical appearance varies somewhat according to the age of the process. The proximal convoluted tubules are widened. The epithelium presents a honey-comb appearance, some of the nuclei being well preserved, others destroyed. Hyalin granular degeneration is apparently less than in the second stage, though fatty degeneration is more marked. The fat is single refracting. The degenerative changes are not so marked in the ascending limb of Henle and the distal convoluted tubules and the honey-comb appearance of the epithelium is here absent. There are a few casts which sometimes take the fat strain in the collecting tubules. The glomerular loops are well filled and the epithelium may here show some fatty change. There is some lymphocytic infiltration in the interstitial tissue though there are no very large areas. The older stages of the process differ from the above in that double refracting substance may be present in the glomeruli and there is marked lymphocytic infiltration in the interstitial tissue with the formation of granulation tissue. In large areas the tubules may be destroyed though the glomeruli in these areas are fairly well preserved, but some show concentric pericapsular thickening. This stage rarely passes over into the fourth stage. Volhard and Fahr have observed only one case of the fourth stage.

FOURTH STAGE.—*Macroscopical.*—The kidneys are much diminished in size; the capsule is adherent; the outer surface is irregular, granular areas of a yellowish color alternating with smooth areas of a dark gray, glassy appearance; the consistency is firm; on cut section the cortex and medulla coalesce; there are dark brown streaks throughout and the markings are obscured.

Microscopical.—The tubules appear as islands surrounded by connective tissue. They are wrinkled and show desquamation and evidence of regeneration of epithelium. Granular and fatty degeneration are less in evidence than in the previous stages. The glomeruli are degenerated by concentric capsular thickening. In some areas there may be increase of capsular cells but generally distinct evidence of inflammation is absent. The heart in this case was not hypertrophied but showed brown atrophy.

The Amyloid Kidney

Formerly there was a tendency to regard the amyloid kidney as a distinct disease both clinically and pathologically. But lately, it is more and more considered an incident in the course of various nephropathies. McCallum states, "In general, then, while some of the symptoms of nephritis are changed by the amyloid in the kidney, we may regard its presence there as incidental, rather than as a cause of nephritis or as constituting a new form of disease." We have seen that the same symptoms are present in nephrosis with and without amyloid. Fahr regards the amyloid kidney pathologically as complicated nephrosis. The same author divides his material of amyloid kidneys into three groups, which he designates as the first, second, and third stages corresponding respectively to the second, third, and fourth stages of nephrosis.

In the first stage, the gross appearance of the kidney is very similar to that of the second stage of nephrosis, though on cut surface it is drier and more opaque. There is a marked difference in the consistency which is decidedly stiff. Only very occasionally is the lardaceous, glassy appearance of the second stage present.

On microscopical examination, granular degeneration is prominent in the proximal convoluted tubules, and fatty changes are about the same as in the second stage of nephrosis. Amyloid is deposited beneath the endothelial layer of the glomerular loops, which are, however, well filled with blood and are permeable. The glomerular epithelium may contain fine particles of fat. The vessels are intact except for the deposits of amyloid. In the interstitial tissue may be seen occasional leukocytes and beginning inflammatory reaction.

The second stage, which corresponds to the third stage of nephrosis, is most frequently encountered, and macroscopically the differences from that of the third stage of nephrosis are quite marked. The kidney is decidedly enlarged, sometimes two or three times the size of the normal kidney. On cut surface the contrast in color between the cortex and medulla may be even more distinct than in simple nephrosis of the corresponding stage. The cortex presents a smuttier gray color.

Microscopically, epithelial desquamation in the tubules is greater, though here the condition with respect to fatty degeneration is about the same. Granular degeneration is more marked and casts are more numerous, especially in the primary collecting tubules. Double refracting lipoids are present in the interstitial tissue as well as in the epithelium. The tubules are widened and lined with very flat epithelial cells. The proximal convoluted tubules are chiefly affected by the degenerative processes.

The glomeruli and capillaries show more marked deposits of amyloid than the previous stage; still many of the glomerular loops are free of amyloid and are well filled with blood. The large blood-vessels are intact and the interstitial tissue shows about the same condition as the third stage of nephrosis.

In the third stage of amyloid kidney, the differences from the fourth stage of nephrosis are still more considerable both macroscopically and microscopically. The kidney is normal or slightly diminished in size. The outer surface is usually smooth, although occasionally slight granulations may be seen. The color is more flecked with brown. On cut section, the cortex and medulla are well contrasted and the markings of the cortex are obscured. The consistency is of marked stiffness and distinctly firmer than in the second stage. The opaque areas on cut surface have a more glassy appearance.

On microscopical examination, the connective tissue increase is diffuse, not focal as in the last stage of nephrosis. The tubules do not appear as islands surrounded by connective tissue, which explains the absence of granules on the surface. The tubules are widened and there are focal areas of small round cell infiltration. In the parenchyma there are areas of degeneration extending in streaks around which there is infiltration of small round cells. While the preserved tubules lie close together here, outspoken island formation, as in chronic nephrosis and in the secondary contracted kidney, is not observed. The initial collecting tubules are wider than in the preceding stage and filled with casts. There is granular degeneration of the epithelium of the proximal convoluted tubules, and conditions with respect to fatty changes are about the same as in the previous stage. The presence of double refracting lipoids is not prominent. The glomeruli are large, filling out the capsule, and show large shadows of amyloid; still some of the glomerular loops are always permeable and well filled with blood. In young individuals the blood-vessels, with the exception of the presence of amyloid, are intact. In old individuals, however, the amyloid is deposited in kidneys, the vessels of which are already affected with arteriosclerosis. Indeed, not infrequently, the amyloid occurs in arteriosclerotically contracted kidneys. Fahr describes two cases, in one of which especially the presence of glomerulonephritis might be considered, but the author concludes that the evidence of glomerulonephritis is not sufficient to classify these cases with those of outspoken glomerulonephritis. Ophuls, however, reports amyloid in secondary contracted kidneys—advanced glomerulonephritis—but in these kidneys there is also present chronic parenchymatous nephritis—the nephrosis of Fahr.

The amyloid kidney, unless occurring in an already arteriosclerotic kidney, is not accompanied by increased blood-pressure and cardiac hypertrophy.

Necrotizing Nephrosis

(*Bichlorid Kidney*)

Symptomatology.—Clinical History.—In poisoning by mercury, one would expect degeneration of the epithelium of the kidney tubules in its purest form, and it might be surprising how the clinical manifestations in these cases differ from those described above as characteristic for nephrosis. In the bichlorid kidney there is not marked edema, there is frequently anuria, the kidney function is often markedly impaired—high non-protein nitrogen in the blood, low phenolsulphonephthalein excretion, manifestations of uremia, and finally slightly increased blood-pressure. The clinical manifestations, laboratory findings, etc., may be illustrated in the following actual incidence:

Case History.—Mrs. ———, thirty years of age; housewife.

Anamnesis.—Family history negative. No serious illness in past history. Two children. Domestic infelicity. At about 8 p. m., May 31, 1916, patient swallowed 52.5 grains (3.4324 grams)—seven 7.5 grain tablets—bichlorid of mercury dissolved in a glassful of water. The patient vomited and complained of pain and burning under the sternum. Her physician was called immediately. He reached the patient in about fifteen minutes. The stomach was washed out thoroughly with milk. Vomiting continued at intervals through the night and there were mucosanguinolent discharges from the bowels. Urine was voided during the night, the last time just before day. The patient was admitted to the hospital at 5 p. m., June 1, 1916.

Status Præsens.—A well-developed, highly cultivated lady, in a good state of nutrition; very weak, but anxious to recover. The mucous membranes of the mouth and throat were very red. She complained of soreness of throat, difficulty in swallowing, burning under the sternum and griping pains in the abdomen. There were frequent discharges from the bowels—mucus and blood—with tenesmus. The temperature was 100.4° F. (38° C.) and pulse 110.

For nine days there was great weakness, depression, much nausea and vomiting, frequent bowel movements—six to twenty-seven daily—backache, headache, twitching of the muscles, delirium and hiccup. On June 8 there was very severe hemorrhage from the stomach and bowels. There were severe salivation and stomatitis. During this time there was no edema; later slight puffiness of the face developed.

Urine.—There was complete anuria from June 1 to June 9. On the latter date, about 150 c.c. were voided. It was of a pale greenish tinge, specific gravity 1012, faintly acid in reaction; there was a trace of albumin; the centrifuged specimen contained a few red blood-cells, leukocytes, many degenerated epithelial cells, broad and narrow finely granular and epithelial casts. It rapidly increased in amount as follows: June 10, 450 c.c.; June 11, 1190 c.c.; June 12, 1395 c.c.; June 13, 1500 c.c.; June 14, 2580 c.c.; June 15, 2250 c.c.; June 16, 1650 c.c., and continued at about this quantity for the twenty-four hours until discharge. On June 16 the phenolsulphonephthalein excretion in two hours was 20 per cent.

Blood.—On June 3—three days from onset—the total non-protein nitrogen was 101 mg. per 100 c.c.; June 8, Hgb. 30 per cent. (Tallqvist); June 21, Hgb. 35 per cent. (Tallqvist); erythrocytes, 1,584,000; leukocytes, 12,600; polymorphonuclears, 82 per cent.; small lymphocytes, 19 per cent.; large mononuclears, 9 per cent.; and eosinophils 0.

Blood-pressure.—On June 2, the systolic blood-pressure was 135, diastolic 80; June 8, systolic 140, diastolic 80 (before the severe hemorrhages); and on June 10, systolic 120, diastolic 55. The patient was discharged from the hospital July 7, 1916. At that time the urine showed specific gravity 1021, no albumin, no casts. Her recovery has been complete. She has since given birth to a baby without any ill effects.

In marked contrast to nephrosis, edema is rarely observed in the mercury kidney. However, Volhard and Fahr report a case in which the edema was a marked feature in a child, the result of calomel medication, and cite a case of Ascoli where the edema was also marked; in this case the poisoning resulted from breathing the air of a room in which bichlorid had been freely used for disinfection purposes. They suggest that these cases may serve to bridge over the gaps from the mild cases to those severe cases in which necrosis of the kidney epithelium is rapidly produced. This view may also be supported by a study of the urine in difficult cases. In mild cases, polyuria without following oliguria or anuria may occur. In severe cases the oliguria may result with high degree of albuminuria as in nephrosis. While in still severer cases an oliguria may precede the anuria which may continue until death or be succeeded by an hyposthenuria. In the period preceding and following the anuria, the urine is of low specific gravity with low nitrogen and sodium chlorid concentration.

The condition of the blood-pressure also varies. In the cases with anuria and azotemia it is usually high and is probably due to the increased nitrogen retention in the blood.

It is often difficult to tell whether certain symptoms, as the gastro-intestinal symptoms, great asthenia, muscular twitching, stupor, etc., are to be referred to the uremia or to the poisonous effects of the mercury. Convulsions and psychoses rarely occur, though Foster has reported the occurrence of these in one case.

Treatment.—It is questionable whether milk has any antidotal effect. Also it should not be forgotten that mercury is soluble in excess of **egg albumen.** Fantus suggests **sodium phosphate** and **sodium acetate** as antidotes. If sodium phosphate cannot be obtained, he substitutes the following solution: **sodium hypophosphite,** 1 gram (15.43 grams), water 10 c.c., **hydrogen peroxid** solution, 5 c.c.

The antidote should be administered at once—the white of one egg to each 4 grains (.26 gram) of mercury, or the hypophosphite in ten times the amount of mercury. The stomach should be thoroughly washed out; it may be repeated if deemed necessary.

If anuria sets in, it will be desirable to **flush** out, if possible, the kidney tubules. For this purpose 500 c.c. of **Fischer's solution** may be administered intravenously. (For preparation of solution see treatment of Nephrosis.)

This should be supplemented as suggested by Lambert and King by continuous **proctoclysis** of 1 dram (3.9 grams) sodium acetate to the pint of water. To facilitate the removal of the poison eliminated by the stomach and intestinal tract, **gastric lavage** and **high colonic irrigation with plain water** may be resorted to twice daily. As demulcent drinks **starch water, slippery elm** or **flax seed tea** may be given at frequent intervals. The duration of this treatment will depend upon the rapidity with which the mercury is eliminated. It should be continued as long as mercury can be detected in the urine and intestinal discharges. For this the **method of Vögel** may be used. This consists in the separation of the mercury from its albuminous combination with organic material by treating it with pure hydrochloric acid and subliming it in a sealed tube to form an amalgam on gold or copper foil.

The nutrition of the patient may be sustained by giving the juice of one lemon, two-thirds of a cup of water and six tablespoonfuls of milk-sugar four times a day. This may be alternated with a glass of sweet milk.

If severe hemorrhage occurs, the subcutaneous injection of **horse serum,** 20 c.c., or **coagulose** will be indicated. The horse serum seemed to have a very good effect in the case here reported.

Prognosis.—The prognosis as to life will depend largely upon how long before anuria sets in and how long it continues. Usually the earlier it occurs after poisoning the graver the prognosis. Still in the case reported anuria set in about six hours and continued for eight days.

In the milder cases followed by polyuria or in the more severe cases with characteristic nephrotic urine, recovery is the rule. The prognosis is more doubtful in those followed by a long-continued hyposthenuria. It is often doubtful as to whether death should be attributed directly to the mercury poisoning or to the urinary poisoning—true uremia. Death may result from severe hemorrhage consequent upon the separation of slough in the gastro-intestinal tract.

Pathology.—Heineke and others have shown that the kidneys show characteristic changes in bichlorid of mercury poisoning.

Macroscopical.—The size of the kidneys varies somewhat according to the duration of the poisoning. In the early stage before inflammatory reaction has taken place in the interstitial tissue, they are of average size, later they are somewhat swollen. The capsule strips easily; the outer surface is smooth, the cortex is broad, sometimes welling out of the capsule. On cut surface, the cortex is broadened and of a yellowish color in marked contrast to the dark brown color of the pyramids. The cortical markings are obscure.

Microscopical.—Instead of cloudy swelling, hyalin granular and fatty degeneration of the epithelium of the proximal convoluted tubules, there is necrosis with evidences of regeneration of the epithelium. There is also a tendency to the deposition of calcium in the epithelium. This possibly is greater in those cases with less severe necrosis. These latter cases are more likely to be associated with evidence of inflammatory reaction in the interstitial tissue. The glomeruli do not usually show any evidence of inflammatory changes.

GLOMERULONEPHRITIDES

Etiology.—The present state of knowledge with respect to the etiology of nephritis does not permit a classification on an etiological basis, however desirable this may be. We have seen that the same etiologic factor may at one time produce a nephrosis and at another time a nephritis. In the nephritides we are met by the same unexplainable fact. Scarlet fever may be followed by a diffuse glomerulonephritis or a focal nephritis, nor is there any difference in the clinical history and pathologic anatomy of a diffuse or focal nephritis resulting from a streptococcic infection and a diffuse or focal nephritis in a pneumococcic infection. The cause for each group of nephritis as well as for the subdivisions of each group is so uniform that the etiology for all forms may be considered together.

The idea of a bacterial origin of nephritis is rapidly gaining ground. There is scarcely an infectious disease in which at one time or another a nephritis has not been observed. Yet those diseases especially associated with streptococci and less often with pneumococci have been especially connected with nephritis. Thus, Aschoff mentions as etiologic factors, scarlet fever, anginas, rheumatic fever, pneumonia and other infections with the streptococcus vulgaris. Bacteria have been found in the urine of nephritic patients and it is claimed these bacteria are capable of producing the changes in the urine and in the kidney of nephritis. Volhard and Fahr state that the most important facts with respect to the etiology of nephritis may be summarized in two sentences, as follows:

"(1) The pathogenic cause of every nephritis is almost without exception a bacterial infection.

"(2) The different forms and stages of nephritis have the same etiology."

The nephritis in association with malaria, which is estimated to occur in from 2 to 5 per cent. of estivo-autumnal infections, is probably an exception in which a protozoal infection may be an etiologic factor. Other exceptions are pregnancy, the relation of which to nephritis is not thoroughly explained, and possibly also lead, though this stands in more definite relation etiologically to the sclerosis.

While the greater rôle is assigned to streptococci and a lesser one to pneumococci in the causation of nephritis, the pathogenesis is obscure. The diffuse glomerulonephritides have usually been attributed to the endotoxins of the streptococci circulating in the blood, which thus conveyed to the kidney for excretion produce injury in the glomeruli which excite an inflammatory reaction. Ophüls, however, points out difficulties in the acceptance of this theory. It is, according to this author, difficult to understand how the poisons could ever become so concentrated in the blood that they would produce the intensely inflammatory conditions in the kidney and in no other organs, or the fact that all glomeruli are not affected similarly and simultaneously. Löhlein postulated the embolic origin of focal glomerulonephritis occurring in infectious endocarditis, although he was unable to demonstrate the presence of streptococci in the glomeruli of his material which represented a late stage of the disease. In early cases Fahr and Baehr were able to demonstrate their presence, proving the deduction of Löhlein. Ophüls extends this idea to the pathogenesis of diffuse glomerulonephritis, basing his view on the presence of hyalin masses to be found in the glomeruli of most all cases during the acute stages of the disease. Ophüls regards these masses as the result of thrombosis and subsequent necrosis of the capillary wall which precede the other changes in the glomeruli. He as others, however, has not been able to demonstrate the presence of bacteria in such glomeruli. This, however, according to Ophüls, may be the result of the rapid destruction of the bacteria by the strong bacteriolytic property acquired by the endothelium of the glomeruli in cases of chronic septicemia. It has been observed clinically that the diffuse glomerulonephritides supposedly of toxic origin as a rule develop two or three weeks after the occurrence of the causative disease, as in scarlet fever and angina, while the focal glomerulonephritides, supposedly of infectious origin, develop along with the causative infection.

Another important problem connected with the etiology of nephritis awaiting satisfactory explanation is the evolution of the disease—the progress of the disease from the acute to the chronic stages. That such a progression occurs is attested by the presence of an unbroken series in many cases. The time in which and the extent to which the chronic stages will develop is dependent chiefly upon the intensity of the acute stage and resulting upon this how much functional tissue is left. Yet the question arises as to how the various stages in the process are brought about. Does the primary toxin or infectious agent continue to act until more and more of the functional portions of the kidney is destroyed? The decided tendency of the acute nephritis to heal is against this view. Is the progress due to the fact that with the destruction of much of the functional portion of the kidney, the compensatory power of the preserved portion fails, resulting in more marked azotemia with formation of toxic substances which act as inflammatory irritants? The occurrence of albuminuric retinitis and the inflammation of serous membranes late in the disease would tend to support this, although this does not seem to offer an adequate explanation. Finally are the end results due to repeated insults to the kidney, as seems to be the case in some cases of so-called chronic endocarditis, chronic arthritis, chronic anemias, and the like? All of these questions await a satisfactory answer.

The following table from Volhard and Fahr show some of the important etiologic relations of the infectious diseases to the two groups of nephritis and their various subdivisions:

Synopsis of the Etiology of the Nephritides

	A. Diffuse Nephritis			*B.* Focal Nephritis				Total
				(*a*) Glomerular		(*b*) Interstitial	(*c*) Embolic	
	Acute Stage	Chronic Stage	End Stage	Acute	Chronic			
Angina	17	7	13	11	4	1		53
Scarlet Fever.....	10	2		6	4	4		26
Infected Wounds..	7	3	1	2	2	2	2	19
Erysipelas	1		1	3				5
Rheumatic Fever and Endocarditis	2	1	2	1			5	11
Purpura				1				3
Cold, Influenza-like Diseases....								
Otitis, Rhinitis....	8	5	6	1	3			23
Pneumonia								
Bronchitis								
Empyema								
Pleuritis	6		1	3		3		13
Tuberculosis	3	1		1	1			6
Gastro-enteritis ...								
Weil's Disease....		1		2				3
Malaria		1						1
Lead Poisoning...			3					3
Pregnancy	4	2	1					7
Unknown	2	9	10	1	2		1	25
Total	62	32	38	32	16	10	8	198

From this table is seen the marked prominence of bacterial infections in etiology of nephritis in 161 of 179 cases in which the cause was known. The great importance of streptococci in particular is shown by the frequency with which these diseases such as tonsillitis, scarlet fever, infected wounds, erysipelas, rheumatic fever and endocarditis, purpura, sinus infections and otitis media, in which streptococci are present, occur in connection with nephritis. Angina occurs as the primary disease in one-fourth of all cases. When it is considered that the tonsils and the pharyngeal lymphatic ring are the portals of entry in the diseases here referred to streptococci, it is seen that these structures are primarily infected in about three-fourths of the cases of known cause—147 in 179 cases. Infected wounds are apparently the cause in 17 cases. The illustrative case reported in connection with acute diffuse glomerulonephritis is clearly due to a streptococcic infection of the hand. From the table erysipelas would seem to be a less frequent cause of nephritis. The author recalls a case in which acute diffuse glomerulonephritis developed in the course of facial erysipelas. The case gradually progressed to the end stage of diffuse glomerulonephritis and death resulted from uremia in about five years after the onset of the acute nephritis. Pneumococcic infections are also infrequent, though Volhard and Fahr state that they form a relatively large proportion of admissions into hospital.

The table shows the relatively great importance of tonsillitis and conditions likely to be associated with persistent streptococcic infection such as the influenza-like diseases, otitis media, and sinus infection in the causation of the end stage of diffuse glomerulonephritis as well as the infrequency with which the end stage occurs in cases due to scarlet fever.

PREDISPOSING CAUSES.—*Heredity.*—Almost all authors have mentioned instances in which nephritis has occurred in several members of the same family. Thus, Eichhorst mentions a family in which nephritis occurred in the grandmother, mother, two sons, and one daughter. In one family observed by Herrick there was a history of renal trouble in the parents and several uncles and aunts. In Volhard and Fahr's series there was nephritis in the sibs of two families, so that an hereditary tendency to the development of nephritis has come to be a well-recognized fact.

Cold.—This condition formerly occupied much the same position in the etiology of nephritis that it did in the causation of pneumonia. This was based on several apparent facts. Exposure to cold frequently appears in the anamnesis of cases of nephritis. The opinion prevailed that there was some mysterious relation between the kidney and the skin. Siegel claims to have produced nephritis in dogs by exposing the feet to cold water. There are many facts to discount cold as more than a predisposing factor in the production of nephritis. Thus careful analysis of the so-called cold nephritis will show an infection along with the cold. Experimental results of the application of cold to the skin on the kidney show conflicting results. Koleman-Muller found an increase of diuresis and Wortheimer a distinct decrease of kidney volume and circulation through the kidney.

Trauma.—This occupies much the same position as a cause of nephritis. The wounds form a focus of infection and a portal of entry for the introduction of bacteria or their toxins into the circulation.

Age and Sex.—An analysis of the cases of true nephritis will show that the great majority of cases occur before the fiftieth year of age and they are more frequent in the male than in the female.

DIFFUSE GLOMERULONEPHRITIS

In adopting the subdivision of diffuse glomerulonephritis into three stages, *viz.*, (1) an acute stage, (2) a chronic stage without kidney insufficiency, and (3) an end stage of chronic diffuse nephritis with kidney insufficiency, it is necessary to call attention to some facts which Volhard and Fahr have set forth in connection therewith.

Transitional cases occur which sometimes render a sharp differentiation from the end stages difficult or impossible, while the symptoms of those cases at either end of the series are characteristic enough. Also mixed types of renal disease occur which may obscure the clinical picture.

The outcome of an acute glomerulonephritis which does not heal is a chronic glomerulonephritis. It cannot be stated definitely how frequently this occurs, but depends largely upon the early recognition and proper treatment of the acute stage. It occurs not only in the severe cases, but also in mild cases. Rarely, especially in the severe cases of extracapillary nephritis, is the process so severe as to preclude the possibility of recovery. The glomeruli may be diffusely involved in the inflammatory process and the functional capacity as a whole sufficient as measured by the usual functional tests. So there may be cases of chronic glomerulonephritis which may exist for a long time without impaired functional capacity. There are other cases of chronic glomerulonephritis which by regeneration of the injured part and overwork of the preserved secreting portion may for a long time compensate the destroyed portion. Thus cases may occur, showing for a long time impaired function before passing over into fatal insufficiency.

The separation of the chronic forms is therefore made on a purely functional basis. This does not depend entirely upon the length of time in which the disease has existed. The end stage may arise directly from the acute stage, especially in the severe extracapillary forms of the disease or gradually through the second stage over a long period of time. Nor does the subdivision of these cases depend upon the macroscopical anatomical condition of the kidney, as the function may be preserved in a contracted kidney and markedly impaired in a large kidney. Yet the histological examination offers some grounds for the judgment as to function. This depends largely upon the extent to which the normal architecture of the kidney has been destroyed. The most characteristic features of this are the destruction of large numbers of glomeruli and tubules with widening of the remaining tubules lined with flat endothelial-like epithelium, which gives rise to the characteristic diuresis of this stage—polyuria with low fixed specific gravity. The kidney is no longer able to concentrate. Volhard and Fahr, in adopting the old classification of Frerichs, emphasize the fact that they do not do so on a macroscopic-anatomical basis, but on a functional basis purely. In the second stage the kidney may already be contracted and in the third stage the kidney may be smooth or indeed enlarged; nevertheless, the greater number of cases of the third stage show secondary contracted kidney anatomically.

Acute Diffuse Glomerulonephritis

Symptomatology.—CLINICAL HISTORY.—It is well known that acute nephritis following scarlet fever frequently shows a distinct period of incubation, usually coming on in two or three weeks after the infection. This may also be seen in those cases developing from diphtheria and tonsillitis.

The general symptoms of onset are frequently slight and may be overlooked if edema is not associated with them or misinterpreted unless the urine is examined as a routine. The patient may complain of fatigue, exhaustion, anorexia and increased thirst, or the disease may set in more stormily with chill, fever and vomiting. Eclamptic uremia not infrequently occurs, especially in children, and this occurs independently of the severity of the kidney lesion. Slight degrees of dropsy and markedly increased blood-pressure predispose to convulsions. It is less frequent in those cases accompanied by high grade dropsy, *i.e.*, complicated with nephrosis. True uremia, or that characterized by the symptoms of urinary poisoning, rarely occurs in the acute form, probably due to the fact that the nephritis is usually not so severe as to lead to severe kidney insufficiency.

PHYSICAL FINDINGS.—*Blood-pressure.*—Increased blood-pressure is a characteristic feature of diffuse glomerulonephritis. Its presence in an acute kidney disease establishes the diagnosis of acute diffuse glomerulonephritis unless it be a necrotizing nephrosis associated with anuria. The pressure may be but little above normal or not at all raised in the mildest cases, as also when the nephritis is associated with conditions such as general sepsis and toxic cardiovascular weakness which prevent a general vascular reaction. It may set in rapidly and disappear early, or, as is more frequently the case, rise gradually and recede gradually. While the highest pressures usually correspond to the height of the disease as indicated by the urinary findings, the maximal pressures cannot be said to run parallel to the severity of the disease. In the author's cases the systolic pressures have varied between 130 and 200. Volhard and Fahr saw in 67 cases values from 140 to 160 twenty times, higher values twenty-one times and lower values twenty-six times.

Frederick von Müller expresses the opinion that the same toxic substances that produce uremia may, in lessened concentration, effect the vasomotor center, thus causing a heightened blood-pressure. Ophüls states that the rise of pressure in the subacute form of glomerulonephritis is possibly due to the irritative effect of the same substance or substances which cause the damage to the endothelium of the blood-vessels, the irritation causing an increased tonus in the arterioles all over the body, which forces up the general blood-pressure. The rise of pressure certainly precedes any noticeable general anatomic changes in the small arteries, and may persist for long periods without being followed by any such change. Whether or not the irritation is to be followed by anatomic changes appears to be purely accidental.

Hewlett states that the hypertension of acute nephritis is probably not due to anatomical changes in the heart or blood-vessels. The rise in pressure may be quite rapid and has been observed within forty-eight hours after the onset of an acute nephritis. This, together with the subsidence of the high blood-pressure as the disease improves, indicates that the elevated pressure is due to changes in function rather than in structure. Although direct evidence is lacking, it seems probable that the acute hypertension in such cases is due to a general constriction of the systemic arterioles. Whether this constriction is caused by nervous reflexes from the diseased kidneys, or whether, as seems more probable, it is due to toxic substances, is not known.

It is generally conceded that glomerulonephritis in contradistinction to tubular nephritis is associated with hypertension, and Volhard and Fahr hold that those nephropathies associated with diffuse glomerular changes are associated with increased blood-pressure. As will be seen from the microscopical findings in the kidney of acute diffuse glomerulonephritis, the glomerular capillaries as well as the vasæ afferentiæ are more or less empty of blood, especially during the height of the disease. Volhard assumed that this was due to an angiospastic ischemia. Recently Walter Hülse from Volhard's clinic has brought evidence which strongly supports this theory and demonstrated the fact that the capillaries of the glomeruli as well as the arterioles of the kidney show an increased tonus in acute nephritis. In two cases of clinically acute diffuse glomerulonephritis which came to autopsy, the kidneys were slightly smaller, the capsules stripped easily, the outer surfaces were smooth and small hemorrhagic points were visible. On section, the cortices were swollen, of a clear brownish color, and well differentiated from the medulla. They presented a parboiled appearance; the markings were obscured. Microscopically, the glomeruli were rich in nuclei, containing on an average of from 50 to 70 leukocytes. The endothelial nuclei were large, swollen, and increased in number. The glomerular capillaries were widened and filled with loose granular masses in which a rare blood-cell was enclosed; here and there was a glomerulus whose capillaries were completely filled with red blood-cells and here the capillaries themselves were almost completely hyalinized.

In the other loops there was only occasional hyalinization. The vasæ afferentiæ did not contain any blood, were partially widened and contained coagulated plasma. The intertubular capillaries were almost wholly empty of blood. The small veins were distended with red blood-cells. It was supposed that if this closure of the vessels were due to increased functional tonus during life, at death this would disappear and it would be possible to inject them under a pressure which did not exceed the blood-pressure during life. Hülse was successful in this in both cases, whereas in a case of diffuse glomerulonephritis with subacute course, marked endarteritis, a blood-pressure of 210 mm. Hg., and which ended from kidney insufficiency, the vessels could not be injected, showing that the closure was of an organic nature. Hülse concluded that the cause of the ischemia in the first stages of acute diffuse glomerulonephritis is not organic, but due to functional spasm which involves the capillaries of the glomeruli as well as the arterioles of the kidney.

Whether the anatomical changes which occur in the vessels and glomeruli in the further course of diffuse glomerulonephritis are to be regarded as the result of this increased tonus must be determined by further examinations. It may be assumed that the arterioles in other parts of the body are similarly affected. The actual cause of the constriction remains undemonstrated.

The Heart.—The findings with respect to the heart vary greatly. In cases with high blood-pressure and slight edema, the apex beat may be displaced downward and outward, the area of cardiac dulness increased, the second aortic sound accentuated, and a presystolic gallop rhythm and a systolic murmur at the apex may be present. Indeed, in rare cases, marked dyspnea and edema of the lungs, the result of cardiac dilation, may dominate the clinical picture. As a rule, however, no signs of cardiac hypertrophy or dilatation can be made out. This is especially likely to be true in the cases combined with nephrosis. It is now generally agreed that the cardiac hypertrophy is the result of the increased work, produced by the increased peripheral resistance. It is said that if an increased arterial pressure lasts for more than four weeks, an hypertrophy of the heart develops.

Edema.—Edema has long been considered a cardinal symptom of acute nephritis. It will be seen from the foregoing, that it is to be regarded as a manifestation of nephrosis rather than nephritis. Many cases of acute nephritis run their course, end in recovery or death in the acute stage or pass over into the chronic stage and finally result in death from kidney insufficiency without showing any edema. Volhard and Fahr have shown by comparing the clinical with the anatomical findings that there is a distinct relationship between the dropsy and the hyalin granular and fatty degeneration of the epithelium of the proximal convoluted tubules, and hold that when dropsy, to any considerable extent, occurs in acute diffuse glomerulonephritis, marked evidence of degenerative changes in the tubular epithelium is present. They designate these as the "mixed type," nephritis plus nephrosis. They state further that about one-half of the cases will show this mixed type. Slightly more than 50 per cent. of the author's cases have shown clinically the combination of nephritis and nephrosis. Slight puffiness of the eyelids or moderate degree of generalized edema not infrequently occurs.

The Eye-grounds.—Changes in the eye-grounds are not nearly so frequent in acute as in chronic nephritis. A true papillitis may be present, and the true albuminuric retinitis is not infrequently found in the cases associated with pregnancy and excessive blood-pressure, as well as hemorrhages into the retina.

LABORATORY FINDINGS.—*Blood.*—Although the patients usually present a pallor of the skin, the blood examinations do not regularly show an anemia. An hydremia is not infrequently present and those cases accompanied by severe dropsy show the clinical and physical changes in the blood-serum described in nephrosis.

Urine.—The color of the urine varies greatly according to the presence of blood. The latter is usually present, especially in the beginning of the process and gives to the urine a smoky appearance. It may also be present in the decline of the process, which indicates an opening up of the blood passages—the glomerular loops—which as a result of the inflammation had become bloodless. Sometimes the blood is recognizable only on microscopical examination. In the absence of blood, the urine is usually paler than normal. The reaction is almost always acid. The quantity is usually greatly diminished. An oliguria of a few hundred cubic centimeters in twenty-four hours may be present and in the severe cases anuria may occur. The specific gravity is usually below normal—the lower it is with oliguria the more severe is the injury to the kidney. Albumin is generally present and varies greatly in quantity. It is, of course, abundant in the presence of macroscopical blood, and also tends to increase as the nephrotic element enters more prominently into the case. It also increases with the occurrence of eclamptic uremia. In the absence of blood, the purer the glomerulonephritis process the less the quantity of albumin. In some very severe cases albumin may be present only in a trace or, indeed, absent. The sediment will show on microscopic examination red blood-cells, casts of various kinds, and frequently bacteria. In the cases complicated with nephrosis fatty epithelium and double refracting substance may be found. Not infrequently the patient complains of pain and tenderness on voiding. Nycturia may also be present, due possibly to the nocturnal elimination of edema.

SPECIAL EXAMINATION.—*Functional Tests.*—The functional capacity of the kidney in acute diffuse glomerulonephritis varies greatly according to the severity and character of the lesion. The ability to excrete water is often not at all impaired and indeed may be excessive with disappearing edema. On the other hand, the excretion may be prolonged or markedly diminished. The same obtains with reference to the ability to excrete salt. The ability to concentrate may be good or impaired. The urea or non-protein nitrogen in the blood is often within normal limits. Slight excesses are, however, not infrequent, and indeed high values may be found. The same variations may be found with respect to the excretion of phenolsulphonephthalein.

Complications and Sequelæ.—Secondary infections do not play such a prominent rôle in pure acute glomerulonephritis as in nephrosis, but erysipelas, pneumonia, pleurisy and meningitis may occur as complications. The outcome of those cases not ending in recovery is chronic glomerulonephritis. With respect to the association with other diseases and the types of the disease it is only necessary to repeat what has been said with reference to the association with nephrosis and the description of the clinical history.

Treatment.—PROPHYLAXIS.—All of those conditions which may give rise to acute diffuse glomerulonephritis should receive careful consideration and appropriate treatment. While every focal infection does not produce an acute nephritis even where they are found definitely to exist, they should, if possible, be removed. In the discussion of the etiology of nephritis we have seen the important part which infections about the pharyngeal ring play in the production of nephritis. Possibly many tonsils as well as teeth are unnecessarily sacrificed, but all cases of acute nephritis should be referred to those competent to investigate and treat tonsils, sinuses and teeth. The Lyon-Meltzer method of investigation of the gall-bladder has shown it to be a point of focal infection and it should receive appropriate treatment, as other foci of infection in the gastro-intestinal and genito-urinary tracts. The kidneys should be safeguarded in all cases of scarlet fever. Frequently a **milk diet** and a **saline purge** will, in these cases, prevent the development of a nephritis. These cases should receive especial care during convalescence. The possibility of the development of nephritis in other infections, such as infected wounds, acute rheumatic fever, respiratory infections, malaria, as well as in pregnancy, should be kept in mind and proper care and treatment of these patients carried out.

The lesson taught by the convalescent camps of men discharged from duty during the World War should be utilized by the civil practitioner. When it is shown that in young men of strong constitutions it requires for complete recovery from scarlet fever 77 days, from tonsillitis and sinusitis 34 days, from diphtheria 57 days, from pneumonia 58 days, and from acute tonsillitis 36 days, it will be realized how remiss we have been in relinquishing care of these patients too early.

The indications for the treatment of acute diffuse nephritis are (1) the removal of the cause when possible, (2) the protection of the kidneys, (3) treatment of complications, and (4) supervision of convalescence.

The cause of acute diffuse nephritis is frequently ascertainable and often capable of being removed. The removal of focal infections, the treatment of diphtheria and malaria, and after careful consideration the termination of pregnancy, etc., are in many of these cases the primary indications.

The protection of the kidneys includes a consideration of rest, environment, diet, and the regulation of fluid and salt intake, and the stimulation of other organs capable of relieving the work of the kidneys.

Rest is the first essential in the treatment of acute nephritis. As soon as the condition is discovered, the patient should be placed at **absolute rest in bed.** There should be plenty of fresh air in the room, but protection from chilling and draughts is necessary. Protected by such clothing as will promote the action of the skin, a part of each day with the patient in the **open air** is desirable. It is often difficult to decide as to how long the bed rest should be continued. Here the best criteria are possibly the condition of the urine as to blood and that of the kidney as to function. Von Noorden has long advised that the presence of blood in the urine was an indication to keep the patient in bed. As a general rule this advice should be adhered to, but we sometimes meet with cases in which hematuria persists and in which the renal function is good. The general condition of such patients, as a result of prolonged rest in bed, may seem to come to a standstill or show distinct evidences of growing worse. In such cases short intervals out of bed each day, with careful watch as to the hematuria and renal function, will result in general improvement. Again other cases are met with in which the blood disappears from the urine, but the kidney function continues impaired. In such cases, rest in bed should be continued unless the general condition seems to be made worse by confinement to bed, when the patient may be allowed to be up a part of each day, exercising the same caution as described above with reference to persistent hematuria. The average case will require a period of from two to six weeks in bed. The return to normal activity should be gradual and controlled by the examination of the urine and the determination of the kidney function.

Von Noorden has pointed out that protective therapy in general is intended in the first place to save the diseased organ all superfluous work, and in the second place to eliminate all those irritants from the diet that might stimulate it to increased effort; but it must always be remembered that protective therapy directed toward sparing one organ should never go so far as to indirectly damage some other organ or the organism as a whole. Hence, while the kidney should be protected by a **low protein diet,** this should contain sufficient caloric value and balance to maintain the nutrition of the patient.

Where the onset is with severe nausea and vomiting, all food by mouth should be withheld and one pint of a 20 per cent. **glucose solution** administered by the drip method **by rectum** every eight hours. Water is necessary in this condition to prevent injurious dehydration of the body. In those cases associated with marked kidney insufficiency the protein should be eliminated from the diet entirely for a short time. The protein-free diet advised by Chase serves very well here. "The juice of one-third lemon, one teaspoonful of cane sugar, six tablespoonfuls of milk sugar, and one glass of water mixed well, may be taken four times a day." This should not be continued more than three or four days consecutively, for after this time on this diet, the patient will begin to draw on his own body proteins. In the average case, the articles of food suggested by Von Noorden may be used. These are milk, rice, groats, maizina or other cereals (made into soup, porridge or pudding with a part of the milk and cream, and with butter and sugar), bread, and fruit juices, particularly sterilized grape juices. The following menu given by Von Noorden may serve as an example from which similar diets may be constructed by any one by reference to any of the numerous food lists with their nutrition value:

Milk (skimmed)	1500 c.c.
Cream	375 c.c.
Rice	50 grams.
Zwieback	50 grams.
Butter	50 grams.
Sugar	20 grams.

This menu contains 2,900 calories. This diet should, however, not be continued for too long a period—possibly not longer than a week or two. With the improvement of the patient the protein content of the diet may be increased, but possibly to not more than 70 grams, in the form of meats, milk, eggs and vegetable proteins for the average man, until all evidence of nephritis has subsided. In the construction of this diet, at this time, due consideration should also be given to its content in carbohydrates, mineral ash and the necessary food substances of unknown chemical nature, the fat soluble A and the water soluble B. All of these substances may be supplied in meat, eggs, the seeds, tubers and green leaves of plants, dairy products and water. Especially during convalescence the difficulty will arise in giving the patient such directions as he is able or willing to carry out to fulfill these requirements. The patient will rarely take the trouble to weigh out the articles of food furnished him. Dr. O'Hare has rendered a great service in the construction of a diet sheet which the patient can use at home and obtain the required constituents of a balanced diet, with great variety and by the use of home measures. The diet sheet is this:

O'Hare's Diet Sheet

Any combination of the foods designated below may be selected.

Foods not listed below must not be taken.

In Groups I and II there is restriction in total amount.

The foods in these groups must be served in full or half portions.

A full portion in Group I counts one. (One is equivalent to approximately 4 grams of prŏtein.)

A full portion in Group II counts two.

In Group III the quantity of each is not restricted, although you are urged to use discretion.

Your total score for the day should be ———.

Your total amount of fluid should be ——— pints.

Do not add salt or spices to the food after it has been cooked.

Group I

(Each full portion counts 1)

Breads	*Full portion*	*Vegetables*	*Full portion*
Bread (white)	1 average slice	Baked beans	1 tablespoonful
Bread (graham)	1 average slice	Lima beans	1½ tablespoonfuls
Uneeda biscuit	5 crackers	Potato, creamed	1 tablespoonful
Shredded wheat	1 biscuit	Potato, mashed	1½ tablespoonfuls
Cereals		Potato, boiled	1½ tablespoonfuls
		Green peas	2 tablespoonfuls
Oatmeal	2 tablespoonfuls	Canned corn	2½ tablespoonfuls
Boiled rice	3 tablespoonfuls	Onion, boiled	3 tablespoonfuls
Cornmeal mush	4 tablespoonfuls	Macaroni	4½ tablespoonfuls
Cream of wheat	6 tablespoonfuls	Squash, boiled	5 tablespoonfuls
Farina	6 tablespoonfuls		

Group II

(Each full portion counts 2)

Dairy Products	*Full Portion*	*Meats*	*Full Portion*
Milk	1 glass	Chicken, roast	3″ x 3″ x ⅛″
Egg	1 egg	Lamb chop, broiled	⅔ chop
Eggs, scrambled	1½ tablespoonfuls	Lamb, roast	3″ x 2½″ x ¼″
Custard	3 tablespoonfuls	Beefsteak, broiled	2″ x 1″ x 1″
Fish			
Cod, boiled	1″ x 1″ x 1½″		
Haddock, boiled	1½″ x 1″ x 1″		
Oysters	7 oysters		

Group III

(No restrictions)

Vegetables	*Fruits*	*Miscellaneous*
Turnips	Watermelon	Sugar
Carrots	Plums	Syrup
Cabbage	Pears	Candy
String beans	Peaches	Honey
Cucumbers	Strawberries	Maple sugar
Cauliflower	Grapes	Butter
Celery	Apple sauce	Cornstarch
Tomatoes (fresh)	Grapefruit	Arrowroot
Tomatoes (cooked)	Raspberries	Tapioca
Lettuce	Blueberries	Post Toasties
Asparagus	Muskmelon	Maple syrup
	Apples	Olive oil
	Pineapple	
	Prunes	
	Oranges	

The patient should keep a record of his daily menu and submit it to his physician from time to time in order that the latter may determine whether or not he is getting the required number of calories to maintain his nutrition.

When acute diffuse glomerulonephritis is associated with nephrosis or in the absence of the latter the kidney is impermeable to water, the fluid intake should be markedly restricted. On the other hand, when the kidneys respond with diuresis to the fluid intake, as they will not infrequently do, there is no indication for the restriction of water. Such an amount of water as will fix the total intake at 1500 to 2500 c.c. may be allowed.

The conditions are very similar in respect to the allowance of **sodium chlorid.** Where marked edema is present the case should be managed just as one of nephrosis (*vid.*). However, in some cases in which edema is not present, the kidneys will not excrete salt well; in such cases, the salt should be restricted. In any case it is well to insist that the patient does not add extra salt after the food is cooked.

DIURETICS.—Speaking of diuretics in acute nephritis, Von Noorden many years ago said, "I regard such prescribing as radically wrong. These stimulants are, so to speak, whip-lashings. It would be the greatest paradox to economize the work of the kidneys to the utmost possible extent in one direction, and in the other to excite them to increased activity by means of the strongest stimulants we possess." More recently Christian and his co-workers have brought experimental as well as clinical proof of the ineffectiveness and possibly the harmfulness of diuretic drugs in acute nephritis as well as in all other uncomplicated forms of nephritis.

In the absence of complications, diaphoretic measures and drugs are not called for; neither are drastic cathartics. Only mild laxatives to secure the necessary daily bowel movements are indicated. For this latter purpose **cascara, phenolphthalein, petrolatum** or **mild salines** like **sodium phosphate** are sufficient.

TREATMENT OF COMPLICATIONS.—The management of edema, uremia and myocardial insufficiency is that described in the chapter on nephrosis, uremia, and circulatory nephropathies (*a.v.*).

SUPPRESSION OF URINE.—This disquieting complication may accompany marked edema in cases associated with nephrosis, set in with uremia in severe cases, or it may exist for some time with few or no toxic symptoms. Its occurrence under the first two conditions has been discussed. What to do in the last case is often a difficult matter to decide. Many, following the lead of Martin H. Fischer, have claimed successful results from the administration of **Fischer's solution** intravenously with or without previous bleeding. While the author has seen good results from this procedure in necrotizing nephrosis, as in suppression of urine in bichlorid of mercury poisoning, it has always been without results in the few cases of acute diffuse glomerulonephritis in which he has tried it. His own experience has rather been in accord with that of Christian, and he believes that his advice, as that of Von Noorden, is the better; *viz.*, to **restrict the diet** to the milk-sugar mixture, the **fluids** to not more than 800 or 1000 c.c. in the twenty-four hours, to **apply heat** to the **lumbar region** and if toxic symptoms begin to appear, to use **diaphoretic measures, cathartics** freely and, according to the condition present, **phlebotomy.**

CONVALESCENCE.—The diet may now be increased in order to build up the general condition of the patient. The protein content of this, however, should not exceed 100 grams per day for the average man. In anemic cases the administration of iron in the form of **Blaud's pills** or **liquor ferri et ammonii acetatis** will be of advantage. The permeability of the kidney for water should be tested at intervals and when it is good, the advice of Von Noorden to administer large quantities of fluid is of value. If convalescence does not progress satisfactorily, a sojourn at the Gulf Coast, the table lands of Arizona and New Mexico or the foot-hills of Southern California may be of benefit.

Prognosis.—The prognosis of acute diffuse glomerulonephritis is immediately good as to life. Most of the patients completely recover. Death may rarely occur from insufficiency of the kidney as a result of the severity of the injury to the kidneys. Associated conditions as the causative sepsis or myocardial insufficiency may result fatally. Complications or secondary infection such as erysipelas, pneumonia, pleurisy, and meningitis may render the prognosis grave.

As to whether the acute will pass over into chronic diffuse glomerulonephritis will depend mainly upon three factors; *viz.*, the extent of injury sustained by the kidney, the time of recognition, and the treatments.

Pathology.—The macroscopical appearance of the kidneys varies greatly. This is due largely to variability of the serous infiltration, the quantity of blood in Bowman's capsules, the tubules and capillaries and the amount of fatty degeneration present. The weight of the kidney varies from normal to 190 grams. The consistency depends largely upon the amount of serous infiltration present. On incising the capsule the substance may well out. The capsule strips easily, the surface of the kidney is smooth and small pin-point or pin-head sized hemorrhages are almost always to be observed.

In cases where the capillaries are markedly filled with blood and there is much extravasation of the blood into Bowman's capsule and the tubules, the color is brown. With empty capillaries the color tends more to grayish brown and the gray tone may be increased by the pressure of fatty degeneration in the epithelium of the tubules. On cut surface the conditions as to color are much the same as that of the outer surfaces. The cortex and medulla are sharply differentiated from each other, the pyramids being quite dark. The cortical markings are often recognizable but may be obscured. The cortex appears as if cooked. With proper light the glomeruli may be seen as small pale translucent points projecting above the cut surface.

The microscopical appearance is more constant and typical. The criteria are lengthening and widening of the capillary loops of the glomerulus, anemia of the loops and particularly the increase of cells of polynuclear and endothelial types inside the loops.

The glomerular epithelium may show swelling, desquamation and proliferation. According to Löhlein the loops of the glomerulus are usually empty of blood and Fahr confirms this in the fully developed stage, but holds that in the fresh stages the loops may be filled with blood. There may be a disproportion between the amount of blood in Bowman's capsule and the uriniferous tubules.

The contents of the capsular space varies. In some areas there may be desquamated epithelium or red and white blood-cells, or both, while in other areas there is only coagulated albumin. Occasionally fibrin is also seen. In many areas adhesions between the two layers of the capsule may exist.

The tubular epithelium varies as to whether the glomerulonephritis is associated with nephrosis, with which there is diffuse and widespread granular and fatty degeneration involving chiefly the epithelium of the proximal convoluted tubules. Without nephrosis the appearance of the tubular epithelium varies according to the stage and degree of the nephritis. Those proximal convoluted tubules in connection with the more severely affected glomeruli may show fatty and granular degeneration. Pure hyalin casts are rare in Henle's loops and the collecting tubules, while conglomerate masses consisting of coagulated albumin, red and white blood-cells in the form of casts are quite numerous.

The interstitial tissue of the kidney shows very slight round cell infiltration in fresh cases, while in more advanced cases it may be quite marked.

ILLUSTRATIVE CASE No. I.—Dr. C. F., white, male, age 40, physician. Seen at his home in Mississippi, January 15, 1921.

Chief Complaint.—Fever, general rachialgia, nausea, vomiting, duration three days.

Family History.—Negative.

Past History.—Has had no previous illness except an attack of cystitis of short duration about fifteen years ago.

Present Illness.—Three days ago he had a rigor which was accompanied and followed by fever; some difficulty in voiding urine, general rachialgia, nausea and vomiting.

Physical Examination.—The patient is well nourished. Height about 5 feet, 10 inches; weight 190 lbs. Temperature 101.4° F. (38.55° C.). Pulse 96 per minute, full and regular. Blood-pressure 160–90. Head, neck and lungs show no abnormalities. Heart, point of maximal impulse in the fifth intercostal space 8 cm. (3.14 ins.) from the midsternal line. No enlargement of the supracardiac area of dulness. The aortic second is possibly a little accentuated. There are no murmurs present. The *abdomen* is without abnormal findings. There is no tenderness in either costovertebral angle. The examination of the nervous system is negative.

Urine.—Single specimen, though it is stated that the twenty-four hour quantity is scant. Dark, amber; specific gravity 1025; albumin, a trace; sugar, negative; microscopical, hyalin, granular and composite casts; a few leukocytes; rather numerous red blood-cells; bacteria, cocci and motile bacilli.

Blood.—Polymorphonuclears 88 per cent.; small lymphothocytes 5 per cent.; large mononuclears 7 per cent. Blood urea 48.5 mg. per 100 c.c. Under rest in bed, low protein diet and laxatives, he rapidly improved. On January 24, 1921, blood-pressure 140–80; urine, no albumin, a rare cast, no pus or red blood-cells; blood urea 31.5 mg. per 100 c.c. Under two months' rest from practice, a diet not exceeding 80 grams of protein per day and a trip to Cuba, he felt perfectly well and fit. Urine negative, blood-pressure 138–70. About the first of June, after getting wet in a rain, he had an attack, somewhat similar though not so severe, as the one in January. On July 21, he was in the author's office when he felt quite well, though the blood-pressure was 155–80; the single specimen of urine voided, was clear, yellow, acid, specific gravity 1024; albumin and sugar, absent; a few hyalin and granular casts, a few leukocytes and epithelial cells, no red blood-cells. Phenolsuphonephthalein output in two hours and ten minutes, 80 per cent.. Blood urea 24 mg. per 100 c.c.

Diagnosis.—Recurring acute diffuse glomerulonephritis.

ILLUSTRATIVE CASE No. II.—B. W., negro, male, age 35, laborer.

Anamnesis.—Family history, negative. Past history, negative except there was a sore on the penis last year, which was not followed by secondary manifestations of lues. About July 1, 1917, he complained of pain in the third finger of the right hand. The pain, which was dull and throbbing in character, grew progressively worse. At the end of the week his doctor made an incision in the finger on the palmar surface. No pus was obtained. The condition of the finger grew rapidly worse. Patient says that the bone rotted and became unjointed. About this time the entire hand and arm became swollen and he had high fever. About three weeks after the first incision was made the finger was amputated. After this there was gradual improvement. Two or three weeks later patient stated that he began to have shortness of breath, that his feet, legs and abdomen began to swell. This had progressively increased and on this account he was admitted to the Memphis General Hospital, September 12, 1917.

Status Præsens.—Well-developed. There is marked general edema, including external genitalia. The third finger on the right hand is absent, amputated at the metacarpophalangeal joint. Healing perfect, though the hand is swollen and stiff.

Heart.—The apex was not located. The area of cardiac dulness extends 10 cm. (4 ins.) to the left of the midsternal line. There is a soft systolic murmur at the apex, not transmitted. The pulmonic second sound is slightly accentuated.

Lungs.—Negative, except for the presence of fluid in both pleural cavities, more in the right than in the left.

Abdomen.—Ascites. Neither liver nor spleen palpable.

Temperature.—97.8° F. (36.55° C.). Pulse 64. Respiration 24.

Urine.—September 13, 1917, pale; specific gravity, 1010; albumin, heavy; casts; pus cells. September 25, 1917, pale; specific gravity, 1010; albumin, heavy; hyalin and granular casts; no pus cells. October 17, 1917, dark straw-color; specific gravity, 1014; alkaline; albumin, heavy;

no casts. October 18, 1917, dark straw-color; specific gravity, 1014; alkaline; albumin, heavy; no cast. November 11, 1917, pale; specific gravity, 1010; alkaline; albumin, heavy; no casts.

Blood.—October 10, 1917, leukocytes, 7400 per cm.; November 12, 1917, erythrocytes, 4,200,000; leukocytes, 6400; polymorphonuclears, 63 per cent.; small lymphocytes, 34 per cent.; large mononuclears, 3 per cent. Wassermann, negative.

Blood-pressure.—September 21, 1917, systolic, 190; October 8, 1917, systolic, 172, diastolic, 118; October 16, 1917, systolic, 170, diastolic, 115; November 5, 1917, systolic, 145, diastolic, 90.

Functional Tests.—Mosenthal kidney-test diet, November 8, 1917, with disappearing edema.

URINE EXAMINATION

Time of Day	Quantity	Specific Gravity	NaCl		Nitrogen	
			Per Cent.	Grams	Per Cent.	Grams
8–10 A. M.	280 c.c.	1010				
10 A. M.–12 M.	225 c.c.	1009				
12 M.–2 P. M.	215 c.c.	1011				
2–4 P. M.	325 c.c.	1010				
4–6 P. M.	200 c.c.	1008				
Total day	1495 c.c.		.76	11.362	.9	13.45
Total night	1244 c.c.	1008	.8	9.952	.85	10.57
Total 24 hours	2739 c.c.			21.314		24.02
Intake H_2O	1760 c.c.			8.5		13.4
Difference	979 c.c.			12.79		10.62

Weight	Period	Blood	Urine				Ambard's Co-efficient
			Period	24 hrs.	Urea Grams	24 Hours Per Cent.	
65.1	4–6 P. M.	48 mg. per 100 c.c. urea	200 c.c.	2400 c.c.	33.6	. 14	.09

Phenolsulphonephthalein (intravenously) 50 per cent. in two hours. CO_2 tension alveolar air 30 (Marriott). R. ph. 8.2 (Marriott).

Diagnosis.—Acute diffuse glomerulonephritis plus nephrosis.

ILLUSTRATIVE CASE NO. III.—W. F., male, negro, age 23, laborer. Admitted to Memphis General Hospital, March 3, 1921; discharged improved April 4, 1921.

Chief Complaint.—Shortness of breath, pain in the abdomen, swelling of abdomen. Duration of symptoms, two weeks.

Family History.—Father was alive and well at 75 years of age; mother, 45, alive and well. Seven sibs, five alive and well, two died in infancy.

Past History.—Used tobacco moderately and whiskey occasionally. Also coffee moderately. Had Tripper two years previous; rheumatism (?) two years ago; several attacks of sore throat and sore mouth; malaria, one year ago; dislocation of wrist, five years ago; burn above the left elbow one and one-half months ago, infected.

Present Illness.—Three days before the onset of symptoms, he noticed that his urine was highly colored (red), and that he voided from 3 to 4 times during the day and from 8 to 10 times during the night. Onset with chill while eating his lunch. The chill lasted several hours and he felt chilly for two days. The chill was followed by fever and profuse sweating, but he had no nausea or vomiting. He was unable to work. The day following the chill he took calomel and oil with good results. On that day he went to work at 1 P. M. During the afternoon he became wet, went to bed, but felt well. That night and for several nights following, he had night sweats which lasted from 12 P. M. to 5 A. M. On the next day he had headache, but felt fairly well and arose from bed. On the fifth day, he noticed some swelling of the feet and ankles. Two days later, he noticed that his eyes were puffed in the morning and later the whole face. His legs and feet swollen, but the swelling subsided some at night. Then abdomen began to swell. His bowels moved every morning. His appetite was good. His nights were restless. At the time of his admission his urine was clear. Frequency, day from 3 to 4 times, night 2 times. There is no burning or straining on voiding. Two weeks after onset of anasarca he began to have shortness of breath and cough. Dyspnea and cough became so severe that he had to sit up to breathe. Two days before admission he began to bring up frothy sputum streaked with blood. Since onset he has also had some dizziness; pain in his right knee and ankles. Lately he has had no fever and no night sweats in over a week.

Physical Examination.—The patient is a well-developed and well-nourished negro man apparently 25 years of age. His color is black, frame large and expression good. He is resting comfortably in bed. He coughs occasionally and brings up blood-streaked sputum. There is edema of face, head and lower extremities. There is a fine scaling of the skin which is hot, dry and of fairly good texture. *Eyes:* Muscles are good, scleræ of a slightly yellow tinge, the pupils were equal and reacted to light and distance. *Nose:* Flat, a typical pug-nose. Nasal cavities are negative. *Mouth:* Lips were fissured; a pigmented rim around the edge of the gums; the teeth were fair; the tongue was clear, no tremor; the throat was negative. *Neck:* No visible superficial veins, no masses felt, contour normal, no tracheal tug. *Chest:* Expansion on both sides equal. *Lungs:* Excursion good; inspection negative, fremitus normal, no change in the percussion note anteriorly, slightly impaired on the left posteriorly in the region of the angle of the scapula where it approached dulness. Wheezing respiration, râles generalized, but especially numerous in the left infraclavicular region; moist râles over both bases; breath sounds audible over chest, with bronchovesicular breathing at the angle of the scapula with increased voice sounds. *Heart:* Apex not visible; point of maximal impulse in the fifth interspace in the midclavicular line; apex beat of good force but fast, no thrills, cardiac dulness not enlarged, sounds clear, not accentuated, no murmurs. *Abdo-*

men: Contour normal, distended, round, uniformly tympanitic, no masses, kidneys, liver nor spleen palpable. *Extremities:* Edema of feet, ankles, legs, knees and hands. Scar with healed area and two small unhealed areas about left elbow due to a burn; the tissues around the elbow were indurated; there was limited motion of the elbow due to pain in healing areas; traumatic deformity of the left wrist, fingers were short and stubby and showed evidence of hard work.

Nervous System.—Negative. *Genito-urinary:* Prepuce was redundant, inguinal glands were enlarged.

Course.—From March 5,1921, bronchopneumonia, fever, quick pulse, gallop rhythm, great dyspnea, frothy, blood-streaked sputum, patchy areas of consolidation; March 29, complete paralysis of extensors of hand and fingers, wrist drop, due to paralysis of right musculospiral nerve. The edema about disappeared and he was discharged to the out-patient department much improved on April 4, 1921.

URINE ANALYSIS

Date	March 4	March 7	March 10	March 11	March 18
Transparency	Turbid	Turbid	Turbid	Turbid	Turbid
Color	Light amber	Light amber	Light amber	Light amber	Light amber
Reaction			Alkaline	Alkaline	Alkaline
Specific Gravity	1017	1025	1022	1025	1014
Albumin	+ + +	+ + + +	+ +	+	+
Sugar	Negative	Negative	Negative	Negative	Negative
Casts	Fine and granular	Many	Many	Many	Many
Leukocytes and pus	+ +	+ + + +	+	Negative	Negative
Red Blood-cells	Negative	+ + +	Negative	Negative	Negative
Quantity				Night 360 c.c.	Day 390 c.c.

BLOOD ANALYSIS

Date	March 4	March 7	March 16	April 1
Red Cells	3,776,000			3,184,000
Leukocytes	7,700	17,500	18,000	5,000
Polymorphonuclears	70 per cent.	79 per cent.	90 per cent.	51.5 per cent.
Small Lymphocytes	24 per cent.	17 per cent.	8 per cent.	47 per cent.
Large Mononuclears	6 per cent.	4 per cent.	2 per cent.	5 per cent.
Eosinophils				1 per cent.
Wassermann			+ +	

FUNCTIONAL TESTS

Date	March 8	March 24	April 5
Phthalein ...	20 per cent. in 1 hour (Intravenously)		
Blood Urea..	75 mg. per 100 c.c.	38.7 mg. per 100 c.c.	33.3 mg. per 100 c c.
Creatinin ...	4.15 mg. per 100 c.c.	2.75 mg. per 100 c.c.	2.14 mg. per 100 c.c.

BLOOD-PRESSURE

Date	*Systolic*	*Diastolic*
March 4	145	115
March 5	130	115
March 7	146	118
March 8	118	88
March 10	140	100
March 12	145	110
March 16	114	108
March 20	140	100
March 23	140	100
March 24	140	90
March 31	140	108
April 4	122	78

Diagnosis.—Acute diffuse glomerulonephritis, nephrosis, bronchopneumonia, and paralysis of right musculospiral nerve.

ILLUSTRATIVE CASE No. IV.—T. J., male, negro, 44 years of age, laborer. Admitted to Memphis General Hospital, November 14, 1919. Died, November 30, 1919.

Chief Complaint.—Swelling of feet, legs and abdomen, and shortness of breath on exercise.

Family History.—Negative.

Past History.—Pneumonia at 18; malaria several times in early adolescence, none recently; sore on penis ten years ago; gonorrhea, seven years previous.

Present Illness.—The present trouble began about the middle of September with pain in the left side about the lower border of the ribs. There was also anorexia, general weakness, cough and fever, though he continued his work. This condition lasted about two weeks. The side is still painful to pressure and the pain intensified by forced breathing.

Two weeks ago, his feet and legs began to swell. The swelling gradually ascended and soon the abdomen became distended. He was also troubled with shortness of breath which he says is especially marked when he ascends stairs. He has never had an attack similar to the present. There had been no nausea, no pain in the abdomen and no visual disturbance. He had had some tinnitus; at night has cough and fever. No dysuria; nocturia, from 2 to 4 times for the last two weeks.

Physical Examination.—A negro, male, of large stature. He was well developed and well nourished. He lay on the left side, since lying on the right side caused pain in the chest. *Head:* Pupils equal, regular and reacted to light: mucous membranes presented a bluish discoloration; the tongue was heavily coated and indented on the edges; cerebral nerves without abnormal findings. *Neck:* The veins are distended and pulsate, especially marked on the right side. *Heart:* Apex beat not seen nor felt. The right border of cardiac dulness was seven and one-half inches to the right of the midsternal line. The left border can not be determined because of the fluid in the left pleural cavity. Heart sounds not heard in the normal area of the apex, but over the ensiform cartilage and to the right of same. They are fairly distinct and there is a slight systolic murmur with point of maximum intensity one-half inch to the right of the ensiform; the sounds at the base are normal. *Lungs:* The respiratory rate is increased and the excursion markedly diminished on the left side; tactile fremitus was absent over the entire left lung; over the same area the percussion note is flat; Traube's semilunar space is obliterated; the breath sounds over the left were distant, but bronchovesicular; there was bronchophony and whispering pectoriloquy in the left inter- and infra- scapular spaces; there were a few diffuse crackling râles throughout the left lung: the right lung was normal except for exaggerated vesicular breathing. *Abdomen:* Showed the presence of considerable free fluid, flatness in the flanks and above the pubes, tympany on top, and a fluid wave; no pain on pressure, viscera could not be palpated. *Extremities:* Scars on right leg, tibial surface, and on back of left arm; the legs and feet are swollen and pitted on pressure. *Lymph-nodes:* There was a generalized adenopathy. *Reflexes:* Were present in the arm; abdominal absent; knee jerks and Achilles present; no Babinski. *X-ray* examinations of the chest showed area of increased density involving the entire left lung crowding upon the right lung, which was also hazy. The blood-pressure was 115–80. Temperature was slightly above normal; pulse 96; respiration 30. Specific gravity of urine 1020, acid, albumin; red blood-cells.

Course.—During the stay in the hospital there was slight fever with periods of apyrexia. November 21 the abdomen was tapped; 660 c.c. of a slightly cloudy fluid with a specific gravity of 1010 was obtained. The non-protein nitrogen of same was 193 mg. per 100 c.c. On November 28, 1080 c.c. of bloody fluid was aspirated from the left chest. For several days before death, there was marked asthenia, somnolence, twitching of the muscles, hiccup and urinous odor of the breath. He had a left otitis media. The patient died November 30, 1919.

BLOOD-PRESSURE

Date	Systolic	Diastolic
November 15............	115	80
November 17............	115	85
November 18............	100	70
November 20............	105	70
November 26............	120	85

About two weeks before admission into the hospital the patient's blood-pressure taken in the out-patient department was 170–105.

URINE

Date	November 15	November 18
Transparency	Clear	Cloudy
Color	Straw	Straw
Reaction	Acid	Acid
Specific gravity	1020	1020
Albumin	+ + + +	+ + + +
Sugar	Negative	Negative
Casts	Hyalin and granular (many)	Hyalin and large and small (many)
Leukocytes and pus cells	+ + +	A few
Red cells	+ +	A few

BLOOD

Date	November 15	November 18
Erythrocytes		
Leukocytes	7000	7600
Polymorphonuclears	72 per cent.	
Small lymphocytes	23 per cent.	
Large mononuclears	1 per cent.	
Eosinophils	4 per cent.	
Wassermann	Negative	

Functional Tests.—November 19, 1921—Phenolsulphonephthalein 0 in two hours. November 22, 1921 (intravenously) 0 in two hours. November 20, 1921, blood urea 139.65 mg. per 100 c.c. November 26, 1921, blood urea 208.05 mg. per 100 c.c.

Diagnosis.—Subacute diffuse glomerulonephritis (extra-capillary), nephrosis, pleurisy with effusion (left), and otitis media (left).

AUTOPSY REPORT.—T. J., negro, male. Well developed and well nourished; rigor mortis present, but easily broken up; slight frontal alopecia; subcutaneous ulcers on lower extremities from which grayish pus could be expressed; both legs increased in size, and pit on pressure; a small decubitus ulcer over sacrum.

Internal Examination.—*Lungs:* Left pleural sack full of straw-colored fluid; all lobes adherent to thoracic wall by fibrous adhesions, giving lungs a ragged appearance when removed; size about normal; substance engorged with fluid containing many fine bubbles and could be pressed together in hands. *Heart:* About normal size; pericardial fluid not increased in amount; lining smooth; valves intact; musculature firm. *Aorta:* A few patches of intimal thickening throughout length. *Liver:* About normal size; consistency firm; on section, diffuse yellowish brown; small stellate thickenings of capsule on anterior surface of the right lobe causing slight drawn appearance of liver substance; slight fibrous adhesions between under surface of right lobe and omentum. *Gall-bladder:* Negative. *Spleen:* Increased in size; capsule slightly roughened by thickened patches of fibrous connective tissue; consistency firm. No bulging when sectioned; color, dark red. *Kidneys:* Considerably increased in size; capsule strips with ease leaving a smooth surface; yellowish, mottled color; several small cortical cysts, containing clear fluid; cortex, grayish yellow in color, considerably thickened, pyramidal portion dark red and well differentiated from cortex. *Suprarenals:* Normal. *Urinary Bladder:* Distended with urine and stringy mucus. *Penis:* Small stricture in anterior urethra. *Brain:* Appeared normal macroscopically.

Microscopic Examination of Kidney.—Glomeruli, not particularly enlarged, but some increase of cellular elements, leukocytes and endothelial cells. The capillary loops contain very little blood. The intracapsular space is filled with desquamated cells, fibrin and detritus forming in many the half-moon bodies. The epithelium of the proximal convoluted tubules show diffuse granular and fatty degeneration. The same process to a much less extent is seen in the straight tubules.

Anatomical Diagnosis.—(1) Subacute diffuse glomerulonephritis (extra-capillary); (2) nephrosis; (3) left serofibrinous pleuritis; (4) edema and multiple abscesses of lower extremities; and (5) inactive tuberculosis of lungs, liver, spleen and kidneys.

Chronic Diffuse Glomerulonephritis

(*Second Stage*)

As stated above, the separation of chronic diffuse glomerulonephritis into two stages is done on a functional basis. The second stage is represented by those cases in which there is little or no impairment of the function. It is realized that there is a transition from the second to the third stage, when at times differentiation is difficult, but those cases occupying either extreme of the series are readily recognized.

Etiology.—These cases undoubtedly arise from an acute glomerulonephritis, although the acute stage often passes unrecognized, especially if in the latter edema was absent or routine examination of the urine was not carried out. The etiology of the chronic form is the same as the acute, streptococcic infections play the chief rôle. It usually occurs in the early decades of life and is rare after the fiftieth year of age.

Symptomatology.—The mode of onset is variable. The patient may complain of no symptoms at all. It is frequently discovered in an examination for life insurance or in the course of an examination occasioned by complaints referred to some other trouble. Occasionally a recurring hematuria may be the symptom which brings the patient to the physician. More often the symptoms of the onset are general complaints, such as headache, fatigue, tendency to dizziness and pain in the back. Sometimes an ever-recurring or never-disappearing edema may be complained of. This may be of renal or cardiac origin.

PHYSICAL EXAMINATION.—The condition of nutrition is usually below par, but often good. It never shows the cachexia of the third stage with marked insufficiency.

Blood-pressure.—This is increased. The systolic pressure is more frequently higher than that of the acute stage and lower than the third stage. It may show marked lability, not infrequently reaching normal values with rest in bed or as the result of intercurrent fever or heart weakness. However, on getting up and assuming the usual duties, with the subsidence of the fever, or with the restoration of the cardiac strength it tends to rise again. If the patient is seen for the first time when the pressure is within normal limits, the symptoms and the presence of slight cardiac hypertrophy will enable one to account for it.

Slight cardiac hypertrophy can almost always be demonstrated. It is, however, not so great as in the third stage. It tends to be greater with marked hypertension and the long existence of the nephritis. The left ventricle is more involved in the hypertrophy. As a result of beginning failure of the left ventricle not infrequently symptoms of relative myocardial insufficiency, such as shortness of breath on exercise, paroxysmal attacks of difficult breathing at night, or a feeling of constriction in the chest will be complained of by the patient. Very marked hypertrophy of the left ventricle is unusual unless some cause for the same accompanies the nephritis.

Edema.—Edema is not an essential sign of chronic diffuse glomerulonephritis. All stages of diffuse glomerulonephritis may run their courses without any edema at all. Not infrequently those cases which have shown edema in the acute stage will be free of edema in the chronic stage. There is often slight puffiness of the eyes and face. On the other hand, edema may be quite marked when it will usually be due to one of two causes or to both, *viz.*, an associated nephrosis or myocardial insufficiency.

Uremia.—The symptoms of true uremia or urinary poisoning never occur in the second stage of chronic diffuse glomerulonephritis. Volhard and Fahr state that eclamptic uremia rarely occurs. The author has observed it in 2 of his cases.

LABORATORY FINDINGS.—*Urine.*—The quantity usually corresponds to the fluid intake. The color is normal except in the recurring hemorrhagic form when it will have the appearance of blood. The reaction is acid. Albumin is present but varies very much in quantity. In uncomplicated cases it is usually small in amount, varying from a trace to 1 or 2 per cent. The quantity of albumin is not an indication of the severity of the nephritis. In cases associated with myocardial insufficiency it tends to be present in larger amounts. In cases associated with nephrosis the quantity is always quite large. Microscopically, except in the hemorrhagic form, a few red and white blood-cells are present. Casts of all kinds are found. Fatty epithelial cells are present in cases associated with nephrosis, but may also be present in cases without marked albuminuria and dropsy.

Blood.—Often a mild secondary anemia is present. In none of the author's cases have the red cells been lower than 3,000,000 per cm. In uncomplicated cases the total and differential leukocyte count is normal.

SPECIAL EXAMINATIONS.—Changes in the eye-grounds occur more frequently than in the acute stage but less often than in the end stage of diffuse glomerulonephritis. In cases associated .with arteriosclerosis the retinal vessels may be contracted and tortuous. True albuminuric retinitis may be present. One case reported by Volhard and Fahr showed choked disc.

Functional Tests.—The characteristic feature of this stage is the absence of any marked impairment of the kidney function as shown by the usual tests. Still slight disturbances, such as a slight excess of the quantity of night urine as compared with the day, may be present. This is especially marked in the cases associated with myocardial insufficiency. According to Volhard and Fahr the water test—the time and amount of urine excretion after the administration of 1500 c.c. of water by mouth on a fasting stomach—shows good results, though the half-hour single quantities of urine tend to be less than in health.

The concentration test—the specific gravity of the urine excreted on a dry diet—is good. The specific gravity and salt and nitrogen excretion in uncomplicated cases vary but little from normal; but with nephrosis may vary as in that condition. With the presence of myocardial insufficiency the rather distinct characteristics of that condition are found. (See Nephropathies of Circulatory Origin.)

The phenolsulphonephthalein output and the blood urea are within normal limits in uncomplicated cases. Schlayer's methods, according to Volhard and Fahr, are of little value. The excretion of potassium iodid is usually within the normal time limit, but may be prolonged in cases with or without edema. The lactose excretion may be good, indeed is almost always so, although the increased blood-pressure would seem to indicate the presence of a vascular lesion.

Diagnosis.—The diagnostic features are:

(1) It usually occurs in the early decades of life, rarely after the fiftieth year.

(2) No symptoms at all may be complained of; a recurring hematuria may be the symptom which brings the patient to the physician; there may be general symptoms such as headache, fatigue, tendency to dizziness and pain in the back; finally an ever-recurring or a never-disappearing edema may be complained of which may be either of renal or cardiac origin.

(3) The condition of nutrition is usually below par but often good; it never shows the cachexia of the end stage.

(4) The blood-pressure is increased but may show marked lability.

(5) The heart is moderately hypertrophied.

(6) There is usually present a moderate degree of secondary anemia with pallor.

(7) The urine usually shows a normal quantity and specific gravity, slight albuminuria, casts, and only a few red blood-cells except in the hemorrhagic form. In cases with marked dropsy it may show the characteristics of nephrosis or of the stasis kidney.

(8) Eye-ground changes are more frequent than in the acute stage, but less frequent than in the end stage.

(9) The chief diagnostic feature is the absence of any marked impairment of the kidney function.

(10) Eclamptic uremia not infrequently occurs; in cases associated with atherosclerosis, eclamptic equivalents may be present; but true uremia does not occur.

Complications, Sequelæ and Association with Other Diseases.—Nephrosis is a frequent association. Myocardial insufficiency has been a frequent complication in the author's cases. Arteriosclerosis may be an associated disease or a complication. Among other complications may be mentioned pleurisy, meningitis and bronchopneumonia.

Clinical Varieties.—As stated in the symptomatology one may meet four groups of cases: (1) Those without symptoms and discovered accidentally; (2) the hemorrhagic form with recurring attacks of hematuria; (3) those with general symptoms, such as headache, fatigue, tendency to dizziness and backache; and (4) those associated with edema.

Treatment.—Uncomplicated cases require no more than the institution of measures for the protection of the kidneys. **Rest in bed** is usually not necessary except in those cases associated with an acute exacerbation or in the hemorrhagic form. While ordinary duties may be continued, the **avoidance of great bodily** and **mental fatigue** and **exposure to wet and cold** should be strongly urged. It is desirable that the patient take a diet sufficient to maintain bodily nutrition. The **O'Hare nephritic diet sheet** may be supplied, and a daily score of 20 to 25, *i.e.*, 80 to 100 grams of protein, allowed. The diet taken should be checked up at intervals by the physician to see that sufficient calories are taken to maintain the normal degree of nutrition. Cases associated with nephrosis or myocardial insufficiency should receive treatment appropriate for these conditions (*q.v.*).

Pathology.—The kidney of this stage was earlier designated as the large white or large variegated kidney. It is constantly enlarged, though the enlargement may be slight or considerable. Fahr has noted kidneys of this type weighing 250 grams (8 ounces). The capsule is not adherent. On section the parenchyma wells out. The outer surface is smooth and of a pale gray or grayish yellow to a brownish color. Small hemorrhagic points are almost always to be observed. The cortex resembles the outer surface as to color and the presence of small hemorrhagic foci. Yellowish specks and streaks besides opaque spots may stand out in the gray or grayish-yellow back ground. It is widened and sharply differentiated from the dark pyramids. The cut surface is moist and glistening, and the consistency is softer than normal though does not show the fragile softness of the acute stage.

The microscopical changes dominate the picture. While proliferative and exudative changes inside of the glomerular loops and in the intracapsular space are associated in all cases, these processes usually predominate in one or the other location to such an extent as to justify separation and description of an intracapillary and an extracapillary form. In the intracapillary form the glomeruli are markedly enlarged, often filling out the whole capsule. The glomerular loops contain very little blood and often are quite devoid of red blood-cells. There is a marked cellular increase inside the loops. These cells are both of the leukocytic and endothelial type, though the latter are more numerous. Frequently adhesions and hyalinization of the loops are seen and not infrequently a whole Malpighian corpuscle may appear as a hyalin clump. In the capsular space desquamated epithelium, coagulated albumin, and red and white blood-cells may be seen here and there, though the space is usually empty, so far as it is not filled with the enlarged glomeruli or closed by the adherence of the two layers of the capsule.

The interstitial tissue is in some areas thickened and small cell infiltration is seen, though not to any great extent. The epithelium of the proximal convoluted tubules may contain double refracting substances which may also be seen accumulated in the interstitial tissue, giving rise to the opaque spots seen microscopically. Focal areas of granular degeneration chiefly of the epithelium of the proximal convoluted tubules belonging to the more severely diseased glomeruli may be seen but these changes are not diffuse except in the case of nephrosis. The blood-vessels in young individuals will usually be found intact but sometimes atherosclerotic changes may be present.

In the extracapillary form of chronic diffuse glomerulonephritis the glomeruli are not particularly enlarged, though the cellular elements inside the loops are increased. The loops are more completely empty of blood than in the intracapillary form. Often they are adherent and hyalinized. The chief feature of this form is the proliferation of the cellular lining of the parietal layer of the capsule. The proliferated cells are arranged concentrically and are more or less intimately attached to the parietal layer of the capsule. They form the so-called half-moon bodies which partially fill the intracapsular space and compress the glomeruli. Frequently organization processes are observed which convert the epithelial masses into concentric layered connective tissue in which spaces lined by a cellular layer occur. Leukocytes, blood and fibrin are also present in the intracapsular space. Sometimes these figures are separated from the wall of the capsule and form half-moon circular masses.

Granular and fatty degeneration of the tubular epithelium may be quite marked, but is not so diffuse as in the second stage of nephrosis. Blood and casts are present in the lumen of the tubules as described in the intracapillary form. In some cases the fibrin content is quite marked in the intracapsular space and inside the capillary loops. Various views have been advanced as to the significance of this fibrin. Engel regarded it as a primary inflammatory product. Löhlein considers it a secondary product of the extravasated blood. Fahr has observed that fibrin excretion is not a marked feature in the early stage of the inflammation and holds that in the course of glomerulonephritis fibrin is found on the inflamed layers of Bowman's capsule analogous to the fibrin formation in pleuritis and pericarditis.

Von Kaldeen has described a thrombosing form of glomerulonephritis, characterized by a richness of fibrin in the capillary loops as well as in the vasa afferentia. Cardiac hypertrophy is usually present in chronic glomerulonephritis of the second stage, but does not reach a very high grade. According to Fahr, heart weights of from 400 to 500 grams (13 to 17 ounces) are observed. It is questionable whether kidneys which have reached this stage ever completely heal.

ILLUSTRATIVE CASE No. I—Mrs. F. G. R., white, 45 years of age, married, housewife, seen at the author's office, January 12, 1921.

Chief Complaint.—Dull headache, chilly sensations, occasional fever and general malaise.

Family History.—Father died of pneumonia; mother died of paralysis; seven sibs, three died in infancy, four are alive and well.

Past History.—Measles, pertussis, varicella in childhood. Since early adolescence she has had catarrhal trouble and her hearing has been impaired for several years.

Menstrual and Marital History.—Menstruation began at 16 years of age; is of the 28-day type; duration, 3 to 4 days. She has one child, 15 years of age. She has had no miscarriages. Menopause occurred at 41.

Present Illness.—About twelve years ago she had a prolonged spell of illness which was diagnosed malaria. She took quinin heroically and after some time she was relieved. Had no trouble for four or five years. For several months at intervals she has a general dull feeling, aching of the limbs and shoulders, chilly sensations followed by slight rise of temperature and loss of appetite. She has lost no weight. When she has these attacks she craves something cold and sour to drink. Since her attack 12 years ago she has been unable to take enough quinin because of catarrh and the condition of her ears. Symptoms referable to the circulatory system are negative. She has a slight hacking cough which is aggravated during these attacks. No symptoms referable to the gastro-intestinal system except anorexia. Urinary symptoms are negative. Her chief complaints are headaches and general malaise.

Physical Examination.—She is well-nourished lady. Temperature is 99° F. (37.22° C.). Pulse 120 per minute, blood-pressure 150–90. *Head and Neck:* Eyes, pupils are equal, regular, react to light and distance; movements are normal and show no signs referable to the autonomic nervous system except a positive Rosenbach. The eye-grounds are negative. *Ears:* The hearing is markedly impaired in both ears; there is no discharge. *Sinuses:* The paranasal sinuses illuminate well. *Throat:* Red, though the tonsils are of normal size and nothing can be expressed from them. *Teeth:* Apparently in good condition. The mucous membranes are of good color. The cerebral nerves are without abnormal findings. The neck is negative. *Chest:* Respiratory movements are full and equal on both sides and the lungs are negative. *Heart:* Point of maximal impulse in the fifth interspace, 10 cm. (4 in.) from the midsternal line, no enlargement to the right; the sounds are rather accentuated, no murmurs. *Abdomen:* Abdominal findings are negative. *Reflexes:* Normal, there is no tremor. *Pelvic organs* not examined. *Urine* (Catheterized Specimen): Clear, light amber, acid, specific gravity, 1012, a trace of albumin, hyalin and granular casts, an occasional leukocyte and no red blood-cells. *Blood:* Differential count; polymorphonuclears, 50 per cent.; small lymphocytes, 46 per cent.; large mononuclears, 4 per cent.; red cells normal in shape, size and staining reaction; Wassermann is negative.

Functional Tests.—Phthalein injected intramuscularly shows 75 per cent. in two hours and ten minutes. *Blood Urea:* 34.5 mg. per 100 c.c. *Sputum:* Three specimens negative for tubercle bacilli. X-ray examination of chest does not show evidence of tuberculosis.

Diagnosis.—Clinical, chronic diffuse glomerulonephritis (intracapillary).

ILLUSTRATIVE CASE NO. II.—A. H., negro, female, age 40, housekeeper; admitted to the Memphis General Hospital, March 13, 1921; discharged at her request, March 29, 1921.

Chief Complaint.—Shortness of breath on exercise, swelling of the legs, pain in the scapular region.

Family History.—Father died of tuberculosis; she was not exposed; mother is alive and well; five sibs, all alive and well.

Past History.—In childhood, measles, pertussis and mumps. Since adolescence, chills and fever, influenza in 1919.

Menstrual and Marital History.—Menstruation began at 12 years of age, of the 28-day type; duration, 4 days; dysmenorrhea, in bed two days at onset; four children, normal deliveries, no miscarriages.

Present Illness.—Began with shortness of breath after attack of influenza in 1919; at this time she also had a cough which was nonproductive until last November. She now expectorates large amounts of thin whitish sputum. Two months ago she began to have pains in the shoulders. These came on gradually, but are now lancinating and radiate down each side as far as the costal margin. The feet and legs have been swelling during the day for the past two weeks. The swelling disappears after a night's rest. Nocturia from 2 to 3 times. She has a feeling of constriction over precordial region. At times there is orthopnea. She also complains of anorexia, general weakness, insomnia, loss of weight and constipation.

Physical Examination.—A fairly well-nourished and well-developed negro woman apparently 40 years of age. *Eyes:* Pupils are equal and react to light and distance; conjunctivæ are anemic. *Tongue, Throat and Tonsils:* Negative. *Teeth:* All missing except the six lower front which are in good condition. *Heart:* Apex beat diffuse and heaving; point of maximal impulse in the fifth interspace 11 cm. from the midsternal line; there is a systolic murmur at the apex, transmitted to the axilla: aortic second is accentuated; the pulse is of high tension and the radials are palpable. *Chest:* Normal in contour except for slight depression below the clavicles. Bronchovesicular breathing over the left apex, moist musical râles with impaired resonance and exaggerated voice and tactile fremitus over upper left anteriorly. *Abdomen:* There is edema of the abdominal wall; the abdomen is distended, with a positive fluid wave; the liver and spleen are slightly enlarged and tender. *Extremities:* The skin is dry; scars over the left tibia; edema of the feet and legs. *Reflexes:* Present but sluggish. Sexual organs not examined.

Course.—She remained in hospital thirteen days without fever, the pulse ranging from 84 to 118 per minute. The edema had about disappeared, the systolic murmur persisted and upon her request she was discharged feeling better.

Blood-pressure.—March 17, systolic 200, diastolic, 140; March 21, systolic 195, diastolic 140.

Urine.—March 17, cloudy, straw-colored, specific gravity, 1020, acid, albumin + + +, hyalin and finely granular casts numerous, an occasional pus cell, no red blood-cells.

Functional Tests.—Phthalien (intravenously) 55 per cent. in two hours; blood urea, 18 mg. per 100 c.c.

Blood.—Red cells 3,000,000; leukocytes 9,300; polymorphonuclears 63 per cent.; small lymphocytes 20 per cent.; large mononuclears 15 per cent.; eosinophils 2 per cent.; Wassermann reaction negative.

Sputum.—Three examinations showed no tubercle bacilli.

X-ray.—Shows peribronchial thickening more marked in the left lung.

Clinical Diagnosis.—Chronic diffuse glomerulonephritis second stage (intracapillary), with myocardial insufficiency, and secondary anemia.

Illustrative Case No. III.—J. S., white, male, 46 years of age, laborer; admitted to the Memphis General Hospital, December 24, 1915; discharged, improved, April 3, 1916.

Chief Complaint.—Shortness of breath; general anasarca.

Family History.—Father died of Bright's disease at 72; mother is dead, cause unknown; four brothers are living, in good health; four brothers are dead, cause unknown. Three sisters are dead, one died in infancy, one from measles, cause of death of other one not known.

Past History.—Of childhood diseases he had only measles; pneumonia at 18, the attack lasted about nine days and he completely recovered; from May, 1915, to July, 1915, he had chills and fever; seven years ago he had sudden sharp pains in the back and hips; these were fleeting in character; he did not go to bed nor stop work on account of them; they continued at intervals over a period of five years, during which time he was a laborer in Indiana coal mines. Five years ago both hips were severely bruised, and right shoulder joint was dislocated. He was laid up 6 weeks; he denies any venereal disease; has had hemorrhoids, which protrude, itch and bleed since he was sixteen years of age.

Habits.—He drinks six cups of coffee; chews two twists of tobacco in three days; smokes occasionally; a whiskey or beer occasionally, and gets intoxicated about twice a year.

Present Illness.—Last October for a day and a half would pass about one teaspoonful of blood after urinating. About the first of

November began to have rigors every fourth night, which continued for two weeks. During these attacks had to urinate from 3 to 4 times at night. After two weeks the rigors at regular intervals ceased and would have only an occasional chill. At this time, about December 1st, his feet began to swell. He was passing as much urine by night as by day. These symptoms continued in somewhat increased severity up to admission in the hospital. At this time his face, feet, legs and scrotum were edematous, and he had shortness of breath.

Physical Examination.—Patient is well developed and nourished. *Eyes, Ears and Nose:* Normal. *Tongue:* Slightly coated. *Teeth:* Bad and there is marked pyorrhea. *Cervical Glands:* Not enlarged. *Heart:* The apex beat is in the sixth interspace 10 cm. from the midsternal line; it is strong and no thrills are palpable; there is no enlargement of cardiac area of dulness to the right. The sounds are clear, aortic second accentuated, no murmurs. *Lungs:* The breath sounds are normal and no signs of fluid in the pleural cavities. *Abdomen:* Is distended with gas and free fluid—flatness at the sides, movable, fluid wave, and tympany at the top; neither spleen nor liver is palpable. *Extremities:* Feet, legs and scrotum are edematous. *Urine:* Straw-colored, specific gravity 1020, albumin + + +, small and broad granular casts, an occasional leukocyte and no red blood-cells. *Blood-pressure:* 160–90. *Temperature:* 100° F. (37.77° C.). *Pulse:* 80 per minute.

Course.—The patient was very weak; there was a slight rise of temperature daily to December 30, 1915. The edema gradually disappeared with a markedly increased urinary output. On January 27, he had a chill with rise of temperature and malarial parasites (estivo-autumnal) in the blood. On March 1, 1916, he had an uremic convulsion. He was unconscious for forty-eight hours; after this he gradually improved. March 14, 1916, hemorrhagic retinitis both eyes, typical albuminuric spot in left eye and a beginning of one in the right eye. From about March 17, 1916, he gradually improved and was discharged from the hospital April 3, 1916.

URINE EXAMINATIONS

Date	Dec. 25, 1915	Dec. 28, 1915	Jan. 16, 1916	Jan. 29, 1916	Feb. 2, 1916	Mar. 3, 1916	Mar. 21, 1916	Mar. 31, 1916
Color	Straw	Light	Straw	Amber	Amber	Amber	Amber	Amber
Reaction	....	....	......	Alkaline	Acid	Acid	Acid	Alkaline
Specific Gravity ...	1020	1010	1015	1028	1022	1020	1020	1015
Albumin	++++	+ + +	+ +	+ +	++++	+ + +	+ +	+ + +
Casts	Many	Many	+ +	+ +	+ + +	+ +	+ +	+ +
Leukocytes and pus	+	+	+	+	Negative	+	Negative	Negative
Red Blood-cells ...	Negative	Negative	Negative	Negative	A few	Negative	Negative	Negative

BLOOD

Date	Feb. 29, 1916	March 13, 1916	March 25, 1916
Red cells..............	....	....	....
Leukocytes	....	....	....
Polymorphonuclears	56 per cent.	79 per cent.	78 per cent.
Small lymphocytes.......	18 per cent.	15 per cent.	16 per cent.
Large mononuclears.....	22 per cent.	6 per cent.	6 per cent.
Eosinophils	2 per cent.	....	....
Parasites	Estivo-autumnal	....	....
Wassermann	Negative, Dec. 28, 1915	....	....

BLOOD-PRESSURE

Date	Systolic	Diastolic
February 18, 1916...........	168	..
March 3, 1916..............	158	..
March 7, 1916..............	158	..
March 11, 1916.............	158	..
April 4, 1916...............	110	80

MOSENTHAL'S KIDNEY-TEST DIET

Date	Hour	Nitrogen		NaCl		Non-protein N. in blood	Urine
		Per cent.	Grams	Per cent.	Grams		
Jan. 6–7, 1916	8 A. M.–8 P. M.	1.012	3.885	.88	3.38		384 c.c.
Jan. 6–7, 1916	8 P. M.–8 A. M.	.62	3.98	.582	3.364		642 c.c.
Jan. 11, 1916	9 A. M.					25.1 mg. per 100 c.c.	
Feb. 17, 1916	3 P. M.					54 mg. per 100 c.c.	
Total		.767	7.865	.756	7.748	79.1	1026 c.c.

Clinical Diagnosis.—Malaria estivo-autumal, chronic diffuse glomerulonephritis (2nd stage), nephrosis, uremia (eclamptic), and albuminuric retinitis.

The End Stage of Chronic Diffuse Glomerulonephritis—The Chronic Form with Kidney Insufficiency, Including the Secondary Contracted Kidney

(Chronic Interstitial Nephritis; Secondary Chronic Interstitial Nephritis; Chronic Nephritis without Edema; Secondary Contracted Kidney; Small White Kidney)

This form of Bright's disease occurs more frequently than was formerly thought, due to the fact that many times it was mistaken for the primary contracted kidney since no history supposed to indicate chronic parenchymatous nephritis could be elicited. In the section on etiology attention was called to the fact as to how frequently the previous history in these cases showed the presence of focal infections with streptococci, such as tonsillitis, influenza-like diseases, otitis media, and sinus infection and as to how infrequently a previous history of scarlet fever was present. The great majority of these cases are the outcome of the second stage, but some may rise directly from the acute, especially from the severe extracapillary forms.

Symptomatology.—The mode of onset will, naturally, often be similar to that of the chronic diffuse glomerulonephritis without kidney insufficiency, that is, the disease may for a long time be latent, often exist for many years, when the first subjective symptoms to occur may be those of uremia, or it may be discovered accidentally, the only symptoms indicating kidney insufficiency being nycturia and polyuria.

The tendency to recurrences seen in the second stage is less frequent, though occasionally slight exacerbations with hematuria may occur. The great number of cases are characterized by chronic or periodical general symptoms. Many of these are due to the toxemia resulting from the kidney insufficiency. Among these symptoms most prominent are headaches, dizziness, scotomata, general weakness, fatigability, general nervous symptoms and insomnia. These may disable the patient temporarily and be followed by a period of freedom, which is in turn followed by a return of the symptoms. This periodicity may exist for many years before a fatal outcome; on the other hand, the symptoms may set in first a short time before the end.

Abdominal pain is a symptom not infrequently complained of by the patients; it may possibly be of the nature of an abdominal angina. Stengel and his co-workers have called attention to the frequency with which chronic nephritics complain of abdominal pain.

Symptoms referable to the heart are quite frequently present. These may be those of relative myocardial insufficiency, such as shortness of breath on exercise, periodical attacks of nocturnal asthma, palpitation, etc., or those of complete cardiac decompensation. The latter are as a rule likely to be associated with the outbreak of uremia, when both are due to the impaired ability of the kidney to excrete water.

UREMIA.—True uremia, that form associated with the retention of the end products of nitrogen metabolism is the inevitable outcome if life is sufficiently prolonged.

The symptoms vary in degree and resemble those associated with suppression of urine. Dyspeptic symptoms are anorexia, which may increase to unwillingness on the part of the patient to take anything by mouth, nausea, periodic or constant vomiting, associated with great general weakness and exhaustion. As a result of the polyuria which produces a great drain on the fluids of the tissue, thirst is quite frequently complained of. There may be present dryness and inflammation of the mucous membranes of the mouth and nose associated with macerating hemorrhages. Fetor urinosis ex ore is rarely absent. Hiccup and itching of the skin often increase the nervous irritability already present. There is inability to sleep soundly. The patient often takes short naps from which he wakes with a start. Associated with the nervous irritability fibrillary twitching of the muscles and tendons is often to be observed. Pain over the precordium and side of the chest may be complained of—the result of the pericarditis or pleuritis which is often a manifestation of uremia. These symptoms are not developed in their entirety in every case.

Dyspeptic complaints associated with great weakness may stand in the foreground a long time before the patient with increasing somnolence passes into complete coma. On the other hand, the symptoms may set in with the suddenness of a catastrophe. Eclamptic uremia rarely occurs in these cases. Volhard has observed convulsions in only 5 cases. In one case, these occurred after an infusion of sodium chlorid glucose solution; in a second, after added salt in testing kidney function; in two other cases of subchronic extracapillary nephritis in which death resulted one half and one year, respectively, after the acute nephritis; and in the fifth case a large subdural hematoma was present. Pseudo-uremic symptoms, so-called eclamptic equivalents, may occur in cases associated with arteriosclerosis of the brain, heart and peripheral vessels. At times during fatal uremia, angina pectoris, cardiac dilatation, Cheyne-Stokes' breathing and symptoms referable to the cerebral and peripheral vessels may occur. All of these as well as the symptoms of cerebral hemorrhage and softening are much less frequently encountered than in benign hypertension and this combined with glomerular lesions—the combination form.

PHYSICAL FINDINGS.—In the early stages, the general appearance of the patient may be scarcely altered. With the progress of the disease there is a gradual loss of strength and towards the end a characteristic cachectic appearance is present. The panniculus is scant, the muscles are flaccid and there is marked pallor, a grayish yellow or a yellowish brown color of the skin. The eyeballs frequently protrude, giving the patient the appearance of one suffering from Basedow's disease. The skin is dry as is also the hair, which is brittle and tends to fall out. Occasionally subcutaneous hemorrhages are observed. Hemorrhages beneath and from the mucous membranes also occur. The eyes may be bloodshot. Epistaxis, menorrhagia and hemoptysis may be present.

Blood-pressure.—Increased blood-pressure is an essential finding. It tends to be higher and more constantly maintained than in the first and second stages. Readings as low as 160 to 170 systolic are rare. In 37 cases, Volhard and Fahr report values over 200 in 14 cases and in one case a systolic pressure of 272 was present. The hypertension tends to be more constant and greater the longer the nephritis has existed. In the early stages or less severe cases it may vary as in the second stage, and under conditions, such as great cardiac and general weakness, may reach normal values for a long or shorter time.

There are probably several factors which contribute to the high and persistent increased blood-pressure in this form of nephritis:

(1) With extensive destruction of the kidney filter a permanent increased blood-pressure sets in probably reflexly by contraction of the peripheral vessels (Aschoff).

(2) Hypertension may arise in connection with unknown intoxication which causes disturbance of the central nervous system which we call uremia. This intoxication is not one of retention in the strict sense, though it is most commonly present in those cases of advanced nephritis which manifest marked nitrogen retention. Clinically, it is associated with severe acute nephritis, sometimes at its very onset, besides the subacute and chronic inflammatory affections of the kidney (Janeway).

(3) Not infrequently atherosclerosis of the small vessels of the kidneys is present in the end stage of chronic nephritis. Some have attributed these changes to the hypertension of glomerulonephritis. Fahr argues that if this were so, one would expect to find similar changes in the arterioles of other areas which are subjected to the same pressure. Atherosclerotic changes may occur in the kidney vessels and be entirely absent in other organs in these cases. Therefore the increased blood-pressure, while it may assist, cannot be the essential cause of the atherosclerosis. This cause must arise in the kidney itself and is chiefly of a mechanical nature. Fahr summarizes his views on this question in the following way: In glomerulonephritis, especially in its chronic form, strong functional demands are made upon the vascular system of the kidney in consequence of the disease of the glomeruli accompanied by progressive destruction of the same. This strong demand is the cause of the atherosclerotic process in the vessels, and the atherosclerosis of the vessels of the kidney produces an increased blood-pressure which is superimposed on the primary hypertension produced by the glomerular disease. The more marked the vascular changes are the more will the degree of hypertension and cardiac hypertrophy approach the conditions in the combination form (the genuine contracted kidney).

The Heart.—While there may be a few exceptions, the heart is regularly enlarged in the end stage of chronic diffuse glomerulonephritis. The left ventricle is always primarily involved, though hypertrophy and dilatation of the right heart is not infrequently associated with the left-sided hypertrophy. The degree of the cardiac hypertrophy rarely reaches that seen in benign hypertension and the combination forms. Jores and others have called attention to the difference which exists between the cardiac hypertrophy in the primary contracted kidney—the red granular kidney—and the secondary contracted kidney. The apex beat is usually pronouncedly heaving and felt in or outside the midclavicular line. There is frequently a presystolic gallop rhythm and in cases associated with involvement of the right side of the heart, a systolic or presystolic venous pulse, widening of the cardiac area to the right, the systolic murmur of relative mitral insufficiency, enlargement of the liver, transudates into the serous cavities and edema are to be made out. Arhythmias are not frequent. The orthodiagraphic measurements are increased; on an average median right equals 5.3 cm.; median left equals 10.4 cm.; and longitudinal equals 17.2 cm. The electrocardiographic tracings almost constantly show left-sided preponderance.

The cardiac hypertrophy is probably dependent upon the hypertension, which as we have seen depends upon several factors. Besides the hypertension associated with glomerular destruction, an important rôle is attributed to the vascular changes developing in the course of glomerular nephritis. Fahr was unable to establish an exact parallelism between the intensity of the vascular changes and the degree of cardiac hypertrophy; however, the latter as a rule was greater in those cases in which marked changes in the small kidney vessels was present. Thus in 5 cases in which the total heart weight exceeded 600 grams (9259.38 grains), in 3 marked, and in 2 very marked vascular changes were present. In 9 cases in which the total heart weight was less than 600 grams, only 3 showed marked vascular changes, in 4, vascular changes were present but in variable degree, and in 2, they were slight. Jores has shown that the degree of tissue destruction in the kidney cannot be the decisive factor in the origin of the cardiac hypertrophy.

The accessible arteries are frequently palpable. Marchand has called attention to chronic nephritis as a cause of arteriosclerosis in early life. Views vary greatly as to the importance of mechanical influence, the result of the hypertension and the toxic influence, the result of kidney insufficiency in the production of arteriosclerotic changes in the large blood-vessels. Volhard calls attention to the fact that arteriosclerotic changes in the large blood-vessels are often more pronounced in the end stage of chronic glomerulonephritis than in benign hypertension which would indicate the relatively greater importance of toxic influence.

Edema.—Edema here as in other types of glomerular nephritis is not an essential symptom. Even in cases where the previous history has shown the presence of edema due to an associated nephrosis edema may be present; although nephrosis which manifests itself clinically by the presence of edema may complicate the end stage of chronic glomerulonephritis.

Edema of cardiac origin is quite frequently present and is sometimes difficult to differentiate from renal edema. Enlargement of the liver and increased venous pressure determined by the method of Hooker and Eyster or A. A. Howell, give conclusive evidence for the cardiac nature of the edema.

Laboratory Findings.—*Urine.*—There is regularly a polyuria in these cases. The color is light yellow often clouded by the presence of organized sediment. The reaction is acid. Albumin is usually present in small amount. Microscopically, are to be seen hyalin and granular casts in varying numbers, fatty epithelium and detritus.

The above urinary findings are changed by a complicating myocardial insufficiency or nephrosis when they may assume the characteristics described for these conditions.

Blood.—Secondary anemia is regularly present; it varies greatly in degree, but may be quite marked.

SPECIAL EXAMINATIONS.—*Kidney Functional Tests.*—Impairment of kidney function is the feature which distinguishes this stage from that of the second stage. The degree of functional incapacity varies greatly and there are naturally all stages, from the slight to the severest degrees. One of the first manifestations of insufficiency is a night polyuria (600 c.c. or more) with a low specific gravity. Another early indication of insufficiency is an inability of the kidney to concentrate. This is shown in the fixation of the specific gravity around 1012 in the single portions of urine passed at two-hour intervals during the day; and also in the low specific gravity of the urine while the patient is on a dry diet. In cases not associated with edema the water test usually results poorly.

While the total daily excretion of sodium chlorid may reach the normal quantity on account of the polyuria present, the impairment of salt excretion is shown by the low percentage excretion and by the fact that added portions of salt are excreted over a much prolonged period and may be completely retained. Nitrogen retention is almost as constant as the tendency to a fixation of the specific gravity and a night polyuria. It is not possible, sometimes, to obtain from careful metabolic determinations as to nitrogen intake and output an idea of the nitrogen retained, as a result of the impaired kidney function. In this the quantitative excretion of nitrogen may be sufficient, *i.e.*, may correspond to the intake and yet the kidneys may suffer greatly in this important function, as shown by adding known quantities of urea to the diet which will be excreted only after a prolonged period, and by quantitating the non-protein nitrogen or urea in the blood, which in cases of this group is usually decidedly increased. The author has ordinarily regarded, according to McLean, urea values of 50 mg. per 100 c.c. of blood as high normal. The degree of increase, however, varies greatly, being dependent upon the protein intake and the degree of kidney insufficiency. The other components of the non-protein nitrogen are also found to be above normal.

Lactose excretion is regularly prolonged as is also that of potassium iodid. However, according to Volhard and Fahr these tests are of doubtful value as to diagnosis and prognosis in these cases.

Ophthalmoscopic Examination.—As a rule the eye-grounds show changes. Albuminuric retinitis is quite frequent, though only small hemorrhages and plaques may be present.

Basal Metabolism.—The basal metabolic rate varies. According to Mosenthal and Marks, in some cases associated with marked dyspnea the metabolism rises as high as 50 per cent. above the average. The dyspnea is the factor that produces this change. A rise in blood-pressure, the presence of an acidosis or the existence of even marked impairment of renal function, as measured by conventional tests, does not influence the plane at which metabolism proceeds. The abnormally high metabolic rates occurring in certain nephritics has been attributed to dyspnea and restlessness characteristic of the severe types of the malady; previous fasting and undernutrition may be responsible for some of the low figures presented.

Furthermore, a study of the respiratory quotient makes it evident that the metabolism of proteins, fats and carbohydrates is in nowise disturbed in cases of heart and kidney disease thus far observed in the calorimeter.

Acidosis.—Some acidosis is usually present in these cases as shown by Sellard's test (it requires more than 5 to 10 grams [77.16 to 154.32 grains] of sodium bicarbonate administered by mouth to render the urine alkaline), by the alkali reserve of the blood (Marriott), and by the tension of the carbon dioxid of the alveolar air. Experimentally, MacNider has found that in acute tubular nephropathies there is a disturbance in the acid base equilibrium in the blood, determined by these methods, which precedes evidence of impaired function. With the following chronic nephropathy in some cases consisting in regeneration of the tubular epithelium of a flat, less specialized type and of the production of chronic obliterative and sclerotic changes in the glomeruli, the alkali reserve increases with improvement of kidney function as far as the elimination of phenolsulphonephthalein and the retention of blood urea and creatinin are concerned. Also in dogs with naturally acquired nephropathy consisting of injury of the glomeruli with well-preserved tubular epithelium, the alkali reserve of the blood may be normal with good kidney function. When such animals had an acute tubular nephropathy superimposed on the glomerular disease by the administration of uranium or mercuric chlorid, there was a rapid depletion of the alkali reserve of the blood and an associated decrease in the carbon dioxid tension of the alveolar air. From this it is inferred that the functional capacity of the renal epithelium has more influence on the acid-base equilibrium of the blood than disease of the glomeruli.

In the human tubular nephropathies (nephrosis), we have found neither the alkali reserve of the blood nor the carbon dioxid tension of the alveolar air reduced to any appreciable extent, while in the end stage of chronic glomerulonephritis there may be marked reduction in the alkali reserves (Marriott's method) and in the tension of the carbon dioxid of the alveolar air leading clinically to air hunger. This acidosis is generally regarded as a retention acidosis and often runs parallel with the impaired renal function as expressed by the phenolsulphonephthalein output and the retention of blood urea and creatinin.

Diagnostic Features.—(1) It usually occurs before the fourth decade.

(2) Symptoms may be absent until just before the end; there is not the tendency to recidives or acute exacerbations of the second stage;

edema of cardiac origin is quite frequent, but that of renal origin is rarely present.

(3) There is a constantly maintained high blood-pressure, usually higher than in other forms of nephritis, but under certain conditions exceptions may occur.

(4) The heart shows marked hypertrophy, but is not usually as great as in the atherosclerosis. It is frequently associated with dilatation and the symptoms of cardiac decompensation.

(5) The blood shows marked secondary anemia.

(6) The urine shows polyuria, hyposthenuria, slight albuminuria and cylindruria.

(7) Papillitis and neuroretinitis are the rule.

(8) The chief characteristic of this stage is the impairment of kidney function. There is a day and night polyuria. The two hourly day specimens show a fixed specific gravity around 1012; the night urine, a low specific gravity; there is impairment of the ability of the kidney to excrete water, salt and nitrogen; the phenolphthalein excretion is low, and there is marked retention of nitrogen as shown in the high blood urea and creatinin.

(9) There is true uremia, contracted pupils, digestive disturbances, hyperirritability, and hypersensitiveness of the body musculature with twitching of the same; urinous odor of the breath; dyspnea and hyperpnea, and frequently inflammation of the serous membranes, especially of the pericardium; fall of temperature; apathy; and stupor. Coma is the inevitable end if the patient lives long enough.

Complications, sequelæ, association with other disease and clinical types have been mentioned in the description of the symptomatology, physical findings, etc., and need not be repeated here.

Treatment.—The prophylaxis of the end stage of chronic diffuse glomerulonephritis is that of the prophylaxis of nephritis in general. The realization that most frequently the end stage is the further development of the first and second stages emphasizes the importance of the early recognition of acute diffuse glomerulonephritis and its proper treatment in the prevention of the chronic stage with impaired function. While the findings of chronic foci of infection in any part of the body and their successful treatment can scarcely be expected to remove injury already done to the kidney, we may confidently expect such procedures to check the progress of the inflammatory process in the kidney, which by regenerative processes may maintain or materially improve an already seriously impaired function.

Such **foci of infection** may and should be judiciously **removed**. The author says judiciously, because such procedures undertaken without every safeguard may sometimes precipitate a fatal uremia.

The care of the patients in this stage of nephritis is largely a special problem, depending upon the condition present. In many cases with only slight impairment of functional capacity, the general measures will be those already described for chronic diffuse glomerulonephritis of the second stage. However, the latent cases which present no general symptoms and only nycturia and hyposthenuria as manifestation of impaired function should receive careful attention as to the regulation of the patient's life with reference to rest, occupation, hydrotherapy, diet, etc. In these cases confinement to the house or bed is not desirable, nor should occupation be entirely given up. However, both **physical** and **mental strain** should be carefully **avoided**. An occupation which favors mild, pleasant outdoor exercise is desirable. An **occasional vacation**, favoring relaxation and rest, is to be urged. It may not be necessary for these patients to make a change of climate if this entails hardships in breaking up home ties, but residence in a **warm, equable climate** is an advantage. These patients do not usually do so well in the extremes of altitude—a moderate altitude in places where great extremes of temperature and moisture do not occur is more desirable. If these favorable conditions cannot be taken advantage of, especial protection against the disadvantages which environment imposes should receive great care. Remaining in the house as much as possible during cold damp weather, and, when it is necessary to go out, protection by proper clothing should be impressed on the patient. **Warm baths** are to be recommended; cold baths are contra-indicated. The protein content of the diet should be regulated according to the condition of the kidney function as shown in the blood urea, but equal care should be exercised to see that the diet contains sufficient proteins to prevent catabolism of the body's own proteins, and other foods to furnish sufficient caloric value and balance. (See *Treatment of Second Stage Chronic Diffuse Glomerulonephritis.*)

Cases with acute exacerbations which do not occur so often as in the second stage should be treated as severe cases of acute diffuse glomerulonephritis.

The greater number of these cases will present general symptoms and more marked kidney insufficiency, and should be subjected to periods of **rest in bed** with careful regulation of **diet** and symptomatic treatment. The protein, salt, and fluids should be restricted, unless uremia threatens, in which case the fluids should rather be increased.

For short periods the proteins may be markedly restricted—30 to 40 grams (462.96 to 617.28 grams) or less per day; no extra salt should be added to food after it has been prepared and it should be used very sparingly in the preparation; the fluids should not exceed 1500 c.c. (3.2 pints) per day.

Those cases associated with edema should be treated according to the causative condition—myocardial insufficiency or nephrosis. The same principles and measures described under Nephrosis and the Stasis Kidney should be instituted. Myocardial insufficiency with threatened uremia should receive very active treatment, and the management of uremia is the same as that described there.

Other complications should be carefully watched for and proper treatment for them carried out.

Prognosis.—The prognosis in the end stage of chronic diffuse glomerulonephritis is ultimately bad. It is an incurable disease, but not incompatible with many years of life. Death is most likely to occur from terminal infection, myocardial insufficiency and uremia.

The tests for kidney function may offer valuable information for prognosis (see *Uremia*). It must, however, not be forgotten that these tests may sometimes result poorly from extrarenal factors; *e.g.*, indescretion in diet, acute exacerbation, or the supervention of myocardial insufficiency. Albuminuric retinitis is of bad prognostic omen in these cases.

Pathology.—It has already been emphasized that there may be great difference in the macroscopical appearance of the kidneys in chronic diffuse glomerulonephritis, and that the function may be markedly impaired in large smooth kidneys as well as in small contracted kidneys. In general, however, the kidneys in these cases may be divided in two groups:

(1) CHRONIC DIFFUSE GLOMERULONEPHRITIS WITHOUT GRANULATION. —*Macroscopical.*—The size is diminished, though it need not be considerable; the capsule is usually adherent; the outer surface is perfectly smooth; the consistency is firm; the color is gray or slightly yellowish; no hemorrhages are visible; on cut surface, the medulla is brownish as compared with the cortex but relatively may be said to be pale; there is no sharp contrast between the medulla and cortex; the markings of the cortex are obscured.

Microscopical.—The glomeruli are uniformly involved, and it may frequently be determined whether the intracapillary or extracapillary process had previously predominated. Many are hyalinized as the result of the intracapillary process.

Often a portion of the glomeruli is changed to hyalin masses, while frequently the glomerulus is completely destroyed. Others are nearly destroyed, and the greater number of loops are completely empty of red blood-cells. Only a few show blood containing loops in large numbers and many of them lie at the periphery while the inner loops show hyalin degeneration. In the Malpighian corpuscles there is occasionally hemorrhage into Bowman's capsule. Usually, however, the capsular space is free—especially no epithelial desquamation. *The interstitial* tissue shows diffuse development of connective tissue between the changed glomeruli; that of the medulla is also increased. Fat and double refracting lipoids are present. *The tubules* are destroyed in great numbers; the preserved tubules are usually widened and contain numerous hyalin and granular casts, and occasionally red blood-cells. There is usually no distinct island formation, and granular degeneration is scarcely demonstrable in the epithelium.

The Blood-vessels.—The small blood-vessels show hypertrophic intimal thickening and arteriosclerosis. Changes may be present in the arciform and interlobular arteries but become slight or wholly disappear in the branches of the interlobular vessels. The feature of this form is the uniform involvement of the glomeruli which accounts for the smoothness of the outer surface. This form is much rarer than the following:

(2) **Chronic Glomerulonephritis with Granulation.**—The chief characteristics of this form are (1) that a number of the glomeruli are preserved, (2) regenerative processes occur, and (3) the morbid processes do not usually come to a standstill, but if they do, they flare up on the slightest provocation until finally complete insufficiency leading to death occurs. The clinical history is necessary to determine whether the end stage has developed directly from the first stage or through the second stage. This form usually develops from the large white or variegated kidney.

Macroscopical.—The size varies. The kidney may still be large, but it is to be remembered that the size of the kidney is not necessarily an indication of how much of the parenchyma has been destroyed. The consistency is much firmer than that of the second stage. The capsule is more or less firmly adherent. The outer surface is granular, usually finely; the gray color predominates in the outer surface and in the cortex, but in the latter a brownish flecking may still be very pronounced. Small pin point hemorrhages may often be seen. On cut surface, the limit between the medulla and cortex is never so sharp as in the second stage, but may be distinct. From this small pale granular kidney the brownish red (secondary contracted) kidney finally develops. In this latter the granulations are usually tolerably equal in size, but marked depressions with large elevations may exist. The capsule is thickened and may or may not be adherent. The pyramids are often markedly contracted, but usually they merge into each other. The consistency is tough.

Microscopical.—The picture is quite variable in contrast to that of the chronic nephritis without granulation, due to the destruction of the parenchyma associated with regeneration.

Completely destroyed and severely injured glomeruli are seen along with others whose loops are fairly well filled with blood. In the advanced stage it is more difficult to recognize the intracapillary and extracapillary processes, though desquamated epithelium may be seen in the intracapsular space. Remains of the half-moon structures are evident. Net form strands may extend between the glomeruli and the parietal layer of the capsule. In other areas the glomeruli are changed into hyalin clumps surrounded by a border of intensively stained cells. In still other areas the glomeruli may consist of scantily filled loops, others again are plump and changed into homogeneous masses, which do not present the glassy appearance of hyalin.

These masses are poor in nuclei, although some may contain numerous nuclei of the endothelial type. There are also numerous completely destroyed glomeruli which are difficult to distinguish from the surrounding lesion. Some glomeruli may contain stiff permeable loops and some may be well filled with blood.

The tubules are widened, many grouped in island formation. These regenerated loops form the granules or nodules on the outer surface. The epithelium of the tubules occasionally show granular degeneration, though less than in the second stage. Fatty degeneration may be in evidence. The degeneration of the tubules is probably largely due to the destruction of the glomeruli to which they belong, but there is evidence that this may in part be due to the direct action of toxins. This process is, however, never so marked or diffuse as in nephrosis. *The connective tissue* is much less uniform than in the second stage. There are quite marked changes in the *blood-vessels*—hyperplastic intimal thickening as well as regressive changes.

How this is brought about is a debated question. There is regularly hypertrophy of the heart, but this does not reach the extent which is seen in the primary contracted kidney. Fahr summarizes his views on these questions in the following way: In glomerulonephritis, especially in the chronic form, the vascular system is under marked strain as a result of the glomerular change accompanied by progressive destruction; this marked strain is the cause of the atherosclerosis of the kidney vessels and the atherosclerosis of the kidney vessels produces an increase of blood-pressure which is added to the primary hypertension produced by the glomerular changes.

ILLUSTRATIVE CASE No. I.—C. P., colored, female, age 26, no occupation. Admitted to Memphis General Hospital, September 10, 1919. Discharged November 4, 1920.

Chief Complaint.—Shortness of breath, swelling of feet and legs, anorexia, matutinal vomiting, pain in the lower abdomen, pollakiuria and nycturia.

Family History.—Father and mother dead, cause unknown; 5 sibs, 1 alive and well, 4 dead, cause unknown; no cancer, tuberculosis, syphilis or nervous disease in family.

Past History.—Has had the usual diseases of childhood; a leukorrheal discharge for about one month.

Menstrual History.—Began at 14; has always been regular, of 28-day type, duration from 3 to 4 days.

Present Illness.—Began three months ago with shortness of breath on exercise. She noticed swelling of the feet and legs two months ago; during this time she has had a poor appetite, attacks of vomiting in the morning and pain in the lower abdomen. The patient states that she has had to urinate every 20 or 30 minutes.

Physical Examination on Admission.—Well-nourished and developed female. Facies shows anxious, distressed expression; fairly marked dyspnea; conjunctivæ pale; tongue, central grayish coating, margins furrowed; moderate edema of the face, especially of the eyelids; notable pallor of oral mucous membranes; teeth in good condition, moderate retraction of gums; pupils react to light. *Thorax:* Expansion poor, respiration largely of abdominal type; apex impulse felt most distinctly in the sixth interspace 2.5 cm. (1 in.) outside the midclavicular line; to the right the area of cardiac dulness extends 2 cm. to the right of the right sternal margin and to the left to the anterior axillary line; there is marked accentuation of both aortic and pulmonic second sounds; there is a gallop rhythm; no murmurs are heard. The liver is apparently within normal limits, the spleen is not felt, there is no sign of free fluid in the abdominal cavity. There is edema of the lower extremities. Temperature 99° F. (37.22° C.). Pulse 102. Blood pressure 175–130.

Urine.—Clear, straw-colored, specific gravity, 1007; reaction neutral. Albumin +; hyalin and granular casts + +; pus cells +. Blood, secondary anemia with slight leukocytosis.

Course.—September 13, 1919, patient had two convulsions—one at 2 P. M. and one at 9:15 P. M. They lasted two or three minutes and patient was in a semi-comatose condition for about 15 minutes following each convulsion. During convulsion pupils were slightly dilated and reacted to light, the breathing was stertorous, there was foaming at the mouth from which some blood exuded, probably due to biting tongue; the patient's attention could be attracted by calling her name, but she would not answer questions.

September 14, 1919, patient had three convulsions to-day.

September 25, 1919, patient's condition has improved considerably the last few days; edema has largely disappeared. She complains of no discomfort except nausea due to taking milk. The heart shows gallop rhythm, aortic second sharply accentuated, bell-like quality; lungs are negative.

September 26, 1919, patient feels better; swelling in feet has almost disappeared.

October 1, 1919, patient is in a stuporous condition, breathing heavily.

October 9, 1919, patient sleeps most of the time during the day.

October 14, 1919, patient complains of pain over precordium, her general condition is growing worse, is stuporous, there is a pericardial friction rub and gallop rhythm.

October 15, 1919, over the entire precordium, there is a pericardial friction rub.

October 16, 1919, patient complains of pain over precordium.

October 17, 1919, feet and legs are more edematous, dyspnea increased.

October 18, 1919, patient complains of pains in the legs and much dyspnea.

October 22, 1919, patient not so well; complains of pains in the epigastrium.

October 27, 1919, pericardial friction now much more pronounced, general edema is more marked, especially in the thighs; patient complains of pain in the right side; she seems very uncomfortable.

October 28, 1919, gallop rhythm, arhythmia and pericardial friction rub very pronounced; edema of extremities more marked; patient is stuporous.

October 29, 1919, patient complains of pains over precordium; asthenia very marked.

October 31, 1919, patient is much worse; semi-delirious; respiration Cheyne-Stokes; pulmonic second sound weak.

November 3, 1919, nose bleeds very much, several times a day; incontinence of feces and urine; patient died at 9:15 P. M.; autopsy refused. The temperature was at no time above normal and distinctly subnormal from October 6 to time of death. The pulse varied from 88 to 124 per minute.

BLOOD-PRESSURE

Date	Systolic	Diastolic
September 10, 1919	175	130
October 6, 1919	180	135
October 7, 1919	195	150
October 14, 1919	150	120
October 15, 1919	160	120
October 17, 1919	198	165
October 21, 1919	160	120
October 24, 1919	168	125
October 28, 1919	148	120
October 31, 1919	155	155

Functional Kidney Tests.—September 27, 1919, phenolsulphonephthalein in 2 hours, 10 min., 0; October 22, 1919, phenolsulphonephthalein in 2 hours, 10 min., 0; and October 2, 1919, two-hour specimens of urine show fixation of specific gravity at 1010.

Blood Urea.—September 28, 1919, 262 mg. per 100 c.c. of blood; October 6, 1919, 173.4 mg. per 100 c.c. of blood; and, October 24, 1919, 265.9 mg. per 100 c.c. of blood.

Creatinin.—October 6, 1919, 17.6 mg. per 100 c.c. of blood.

Ophthalmoscopic Examination.—Both fundi show neuroretinitis.

Clinical Diagnosis.—Chronic glomerulonephritis (end stage), myocardial insufficiency, double neuroretinitis, and uremia.

ILLUSTRATIVE CASE NO. II.—A. F., male, negro, age 38, concrete worker; admitted to Memphis General Hospital October 7, 1920; discharged improved, October 26, 1920.

Chief Complaint.—Shortness of breath on exercise, and swelling of feet and legs.

Family History.—Father has rheumatism, right shoulder; otherwise negative.

Past History.—In childhood, measles and pertussis. Post-childhood, malaria, influenza-pneumonia twice, last attack two years ago. Tripper two years ago. Sore on penis 17 years ago. Never had an eruption; says his Wassermann taken at Outpatient Department was negative.

Present Illness.—He has not been well since his attack of influenzal pneumonia two years ago. Three weeks ago he noticed that his feet were swollen. This is worse toward night after he has been on his feet all day. He has headache, precordial pain and dyspnea. He has been gaining some weight in the last week but is weak and does not feel well. He has been spitting up blood at times for the past two weeks.

Physical Examination.—Male, black, well-nourished, 38 years of age. Temperature 98.4° F. (36.88° C.); pulse 84; blood-pressure 220–158 mm.

Hg. Seems comfortable. Eyes, tongue and throat negative; mucous membranes, a little pale. *Heart:* Slightly enlarged to the left; a soft systolic murmur at apex, transmitted toward axilla, not heard in the back; aortic second accentuated; reduplication of pulmonic second; radials palpable; pulse 100 per minute, full and bounding. *Lungs:* Slight dulness beneath the right clavicle; breath sounds diminished to some extent at right apex anteriorly; a few crackling râles heard at right apex and over the left base posteriorly; voice sounds diminished over left lobe posteriorly; other organs without abnormal findings; slight edema of both ankles. *Urine:* Clear, light yellow; specific gravity, 1009, reaction acid; albumin +; sugar, negative; casts + + + (hyalin, fine and coarsely granular); red blood-cells and pus cells negative.

Blood.—Leukocytes, 5,500; polymorphonuclears 74 per cent.; small lymphocytes 15 per cent.; large mononuclears 10 per cent.; eosinophils 1 per cent.; Wassermann, negative.

Functional Tests.—Phenolsulphonephthalein (intravenously), 15 per cent. in two hours.

Blood Urea.—119.4 mg. per 100 c.c.

Diagnosis Clinical.—Chronic diffuse glomerulonephritis (end stage), and myocardial insufficiency.

ILLUSTRATIVE CASE NO. III.—R. H., male, negro; age 25, works in cotton shed. Admitted December 9, 1920; died December 12, 1920.

Chief Complaints.—Bleeding from rectum.

Family History.—Father dead, rheumatism; mother, dead, pneumonia.

Past History.—Measles, mumps in childhood; Tripper in June, 1920. Has had nosebleed before, which lasted two days.

Present Illness.—A few days ago, patient fell backwards on bath tub, since then he has been bleeding from the rectum continuously. The hemorrhage was more profuse the first day. Nose began to bleed on day of admission at 4:30 P. M. and there has been a steady trickle since that time. Bowels act once daily, there is pain in the region of the rectum on emptying the bowel. He also complains of pain in the region of the umbilicus. There is a burning on voiding urine which is of a dark muddy color. The patient is extremely drowsy, he nods between questions and goes to sleep immediately after being aroused

Physical Examination.—Male, negro, 25 years of age, well-nourished. Temperature 98° F. (36.66° C.); pulse 108; blood pressure 178–130 mm. Hg. *Head:* Round, flat face, thick lips, flat nose, edema of eyelids, pupils react to light and accommodation; mucous membranes very pale; tongue broad, thin, covered with a grayish coat, ulcer on lower lip. *Heart:* Apex in the fifth interspace 4 in. (10.16 cm.) from midsternal line, a soft blowing systolic murmur at apex transmitted to the axilla; arteries are soft, pulse rapid and of high tension. *Lungs:* Negative. *Abdominal Organs:* Without findings except umbilical hernia; the skin is cool, dry and scaly. *Bones and Joints:* Negative. *Muscles:* Well-developed and hard. Epitrochlears, cervical and inguinal lymph-nodes are palpable. Reflexes, normal. Blood exudes from the nose and rectum.

Urine.—Clear, pale, straw-colored; specific gravity, 1012; alkaline; albumin +; casts + + (finely granular).

Blood.—Red cells, 2,400,000; leukocytes 8,200; polymorphonuclears 87 per cent.; small lymphocytes 9 per cent.; large mononuclears.

Functional Tests.—Blood urea, 232.2 mg. per 100 c.c.

Eye-grounds.—The nerve heads are pale and there are areas of retinal exudate. Hemorrhage in both eyes near the disk. The macular regions do not show any change.

Course.—One hour after admission, December 9, 1920, patient bleeding from rectum and nose; 10 c.c. of normal serum given; blood-pressure 178–130. Temperature subnormal; rectal examination reveals no cause for hemorrhage. There is no history of hemophilia in the patient's family; 10 c.c. horse serum at 6:00 P. M. December 10, patient has not bled any to-day, is drowsy, sleeping all the time. December 11, 1920, patient had a convulsion last night lasting one minute and another one this morning. The urine is incontinent, he is comatose and the breathing stertorous. December 12, 1920, patient did not come out of coma and died at 12:20 P. M.

Clinical Diagnosis.—Chronic diffuse glomerulonephritis (end stage), secondary anemia, albuminuric retinitis, and uremia.

ILLUSTRATIVE CASE NO. IV.—Horace Martin, male, colored, age 26. Admitted to Memphis General Hospital, October 15, 1921. Died October 21, 1921.

Chief Complaints.—Shortness of breath, and tight drawing sensation in abdomen.

Family History.—Negative.

Past History.—A previous similar attack in July, 1920; otherwise negative.

Present Illness.—The present illness began ten days ago. Onset was gradual. He first had an uncomfortable drawing sensation of stiffness in the legs about ankles and knees. The swelling would disappear after a night's rest. Three days after onset he began to have shortness of breath. He was forced to quit work. There was puffiness about the eyes and abdominal swelling followed. The above symptoms have rapidly grown worse. He has nycturia, 4 to 5 times. He is constipated and has anorexia. No other symptoms.

Physical Examination.—Well-developed, well-nourished negro, male, age 26. Lies quietly in bed; has a very anxious expression on his face and is gasping for breath. Temperature 97° F. (36.11° C.), pulse 70, respiration 18, blood-pressure 190–120. *Head:* Normal contour; hair appears lifeless, is falling out, though not in circumscribed areas. *Face:* Swollen and there is puffiness about the eyes. *Teeth:* Very faulty. *Tongue:* Large and pale; right border is notched. *Tonsils:* Small and ragged. *Pharynx:* Hyperemic. *Neck:* The vessels are very prominent. Cervical and submental adenopathy. *Chest:* Symmetrical in development and respiratory excursions are rapid and not full. *Lungs:* Tactile and vocal fremitus diminished over both bases posteriorly. Moist râles are heard over this area. Breath sounds are harsh at apices. *Heart:* Apex in seventh interspace 1½ ins. (3.81 cm.) inside the midclavicular line. Right border at right border of sterum; left border in midclavicular line. Sounds are very rough, no murmurs. Aortic second accentuated. *Abdomen:* Distended; dulness below stomach. No distinct fluid wave. *Liver:* Palpable 1 in. (2.54 cm.) below costal arch. *Spleen:* Not palpable. The epitrochlear glands are enlarged. The extremities are edematous. The reflexes are normal. The sexual organs are negative.

Urine.—October 16, 1921, color pale; specific gravity, 1010; reaction acid, albumin negative; glucose, negative; casts negative; leukocytes and pus cells a few.

Blood.—Red cells 4,000,000; leukocytes 8,800; polymorphonuclears 75 per cent.; small lymphocytes 21 per cent.; large mononuclears 4 per cent.; Wassermann + + + +. No parasites.

Course.—October 17, 1921, patient dyspneic, generalized edema, tongue anemic, a patchy looking area on right margin. *Heart:* Apex rather diffuse, is displaced inward, is located in the sixth interspace. Cardiac dulness extends to the right of the sterum. Left border of the heart inside the left nipple line. Sounds are valvular in quality with marked roughening; no murmurs; aortic second distinctly accentuated. *Lungs:* Tactile fremitus diminished over both bases posteriorly. Voice and whispered sounds diminished over bases with moist râles. No tracheal tug. *Abdomen:* Tympany above, flatness in flanks. *Liver:* Tender. Dulness from fifth rib to two fingers' breadth below costal arch. *Spleen:* Not palpable. October 18, 1921, no marked change in patient's general appearance, though the impaired pulmonary resonance over bases posteriorly is more marked and the heart sounds are very rough. There is an area of bronchovesicular breathing over the right lower lobe posteriorly. October 19, 1921, an indistinct to-and-fro friction rub heard between the second and fifth ribs to the left of the sternum above crossing to right below, marked orthopnea. October 20, 1921, patient unimproved. Orthopnea, suffering great pain in the chest. A very loud to-and-fro friction rub heard over entire precordium. Heart sounds are distant. Lungs show areas of diminished resonance posteriorly, right middle and lower, an area of tubular breathing over middle of right lobe posteriorly. Abdomen tympany above, flatness in flanks. October 21, 1921, patient gasping for breath, pulse almost imperceptible. Dulness over bases, lower middle right almost completely flat. Patient rapidly on decline. Patient unconscious, cannot be aroused. Died at 10:40 A. M.

Urine.—October 18, 1921, pale, specific gravity 1010, acid, albumin negative, many hyalin (small, large and coarsely granular) casts.

Functional Tests.—October 20, 1921, phthalein 15 per cent. in 2 hours. Blood urea 70 mg. per 100 c.c. Creatin 2.35 mg. per 100 c.c.

Clinical Diagnosis.—Chronic diffuse glomerulonephritis (end stage), myocardial insufficiency, pericarditis, uremia, and bronchopneumonia.

Autopsy Report.—Horace Martin, October 24, 1921.

External Examination.—Body that of a large well-developed, muscular, well-nourished colored male, 179 cm. (5 ft., 10½ ins.) in length. Edema of the face and neck.

Internal Examination.—Small amount of clear straw-colored fluid in the pelvic cavity. Congestion of the capillaries of the small intestines. Clear yellow fluid in both plural cavities. A large amount of slightly cloudy yellow fluid with masses of fibrin in pericardial sac with slight congestion of the serous surfaces. Thymus negative. *Heart:* Greatly enlarged, 580 grams (1.28 lbs.). Walls thickened, left ventricular wall 2 cm. Myocardium reddish brown, firm. All chambers dilated; valves, coronary arteries, pulmonary arteries negative. Aorta and thymus, negative. *Lungs:* Very large, edematous, heavy, less air than normal. On section large amount of rust-colored fluid. *Spleen:* Enlarged 430 grams (.95 lbs.), firm. On section, deep red and level with cut edge. *Liver:* Enlarged, lobulated, externally and on section prominent, center deep red. Gall-bladder and ducts negative. *Kidney:* Small, 110 and 90 grams (.24 and .2 lb.). Capsule adherent, surface finely nodular, gray, firm, cut with resistance, cortex narrow, .4 cm., striations indistinct, blood-vessels not prominent. Pelves and ureters negative. *Stomach and Intestines:* Throughout entire extent, mucous membrane swollen, covered with large amount of gray, granular material. *Bladder:* In mucous membrane are scattered bluish-white translucent nodules 1 mm. in diameter with black periphery, singly or in groups of as many as five in number; their individuality is retained, being freely movable with mucous membrane, most numerous in trigone. Pancreas, mesenteric lymph-nodes, seminal vesicles, testicles, negative.

Bacteriology.—Heart's blood and pericardial sack, negative.

Microscopical Kidney.—Many glomeruli are enlarged, filling the whole capsule in which there is marked intracapillary proliferation. Others show partially destroyed glomeruli in which a part of the loops has undergone hyalinization, while other glomeruli are completely changed to hyalin clumps. There is very little or no proliferation of the capsular epithelium. In places there is quite marked pericapsular thickening. *Tubules:* In many areas there is distinct island formation of the tubules, *i.e.,* dilated tubules lined by a low type of epithelium, surrounded by increased connective tissue. In some areas the tubular epithelium shows some granular and fatty degeneration though this is not marked. Many tubules contain casts. Interstitial tissue is distinctly increased. There are rather large areas of small cell infiltration and old connective tissue is quite in evidence. *Blood-vessels:* There is distinct thickening of the walls of the blood-vessels in the boundary zone. The smaller vessels show distinct arteriosclerotic changes.

Microscopic Diagnosis.—Chronic diffuse glomerulonephritis (end stage), secondary contracted kidney.

Anatomic Diagnosis.—Chronic diffuse glomerulonephritis (secondary contracted kidney), hypertrophy and dilation of heart, general chronic passive congestion, serofibrinous pericarditis (sterile), and bronchopneumonia.

THE FOCAL NEPHRITIDES

Acute Focal Glomerulonephritis.—This usually begins suddenly and simultaneously with the causative infection. As a rule the patient complains of no general symptoms. There may be some difficulty on voiding or pain in the lumbar region. The symptom which usually calls the patient's attention to a disturbance in the kidney is the bloody appearance of the urine. On physical examination, no edema is found, the blood-pressure is not increased, and there is no evidence of cardiac hypertrophy. The urine usually shows a bloody appearance, much albumin due to the blood present, casts and many red blood-cells and leukocytes. Bacteria are often present.

The functional kidney tests are usually good. The quantity is normal, unless reduced as results of fever of the causative infection. The salt, water, and nitrogen excretion is good, and there is usually no retention of urea in the blood. It is quite possible that the focal lesions may be so extensive as to produce marked insufficiency with uremia, as the author has seen in one case.

Uremia in none of its forms, however, occurs as a rule. The absence of eclamptic uremia is explained by the absence of hypertension and dropsy, eclamptic equivalents by the absence of arteriosclerosis in various areas and true uremia by the absence of nitrogenous retention in the blood.

The diagnostic feature of acute focal glomerulonephritis is the presence of hematuria with the absence of increased blood-pressure and cardiac hypertrophy. It may sometimes be difficult to decide between a subsiding acute diffuse glomerulonephritis and acute focal glomerulonephritis, as the following case shows:

Mr. L. S., white, age 34, married, merchant, seen October 30, 1921. Chief complaint, shortness of breath, swelling of feet and ankles, and pain in lumbar region (bilateral). Family history, negative. Past history, pleurisy, chills and fever. Appendectomy 1907. *Present Illness:* About two months ago was hit by a stone, fracturing nasal bone. This was infected and he was operated on. Last week he was taken with severe pain in lumbar region and swelling of face. Later he noticed shortness of breath, breathing being especially difficult at night. Swelling of ankles, knees and chest. Some frontal headache. No difficulty with urination. *Physical Examination:* Temperature 96° F. (36.66° C.); pulse 72; blood-pressure 142–82. Patient is undernourished, rather pale in appearance, slight swelling of the right side of the face. Many crowns and bridges. Throat, red. *Chest:* Possibly slight impairment of motion at right apex. Slight increase of vocal fremitus at both apices.

Pulsation in the vessels of the neck. Bronchovesicular breathing in right suprascapular area, increased whispered voice sounds. A few inconstant râles at left apex. *Heart:* Apex beat in normal position, an occasional extra systole; otherwise negative except for possible slight accentuation of aortic second sound. *Abdomen:* No tenderness; negative. *Knee-jerks:* Active. No edema of extremities. *Blood:* Leukocytes 8000; polymorphonuclears 73 per cent.; small lymphocytes 23 per cent.; large mononuclears 3 per cent.; basophils 1 per cent.; blood urea 64.5 mg. per 100 c.c.; Wassermann negative. *Urine:* Cloudy; amber; specific gravity, 1026; acid; albumin + + +; sugar negative; microhyalin, granular and blood casts; pus cells + + +; red blood-cells.

With rest in bed, on diet restricted to 50 grams of protein, for three weeks the patient felt well, the slight swelling of the face subsided, the blood-pressure returned to 120–70, the blood disappeared from the urine. After being up for two weeks, the urine showed blood macroscopically, specific gravity, 1018, albumin + + + +; no casts; blood-pressure 118–65, and blood urea 45 mg. per 100 c.c. This is an illustration of Volhard's statement that an original acute diffuse glomerulonephritis may recur as the nonhypertonic, focal type. The combination of edema and hematuria without hypertension, generally, is in favor of a subsiding, diffuse glomerulonephritis associated with nephrosis.

The treatment of acute focal nephritis is much the same as that described for acute diffuse glomerulonephritis—**rest in bed,** and **slightly restricted protein diet.** As in acute diffuse nephritis the general condition may grow worse under confinement to bed, when the patient may be allowed to be up and take moderate exercise, provided the hematuria is not increased thereby. Styptics, such as calcium salts, gelatin, ergot, adrenalin, coagulose and lead salts are without any beneficial effect. Sometimes the hemorrhage may be so great and associated with pains in the lumbar region as to suggest the advisability of surgical intervention. In such cases **decapsulation** under local anesthetic with as little handling and trauma of the kidney as possible will be attended with good results. Of course any focal infection present should be removed if possible. The immediate result of such operations is, however, an increase of the hematuria which subsides after a short time.

The prognosis of acute glomerulonephritis is good, except in cases associated with severe sepsis. There is a great tendency for these cases to recur and they sometimes pass over into chronic focal glomerulonephritis.

PATHOLOGY.—The kidney in acute focal glomerulonephritis offers no characteristic appearance macroscopically. As the name indicates, while the changes are of the same character as in the diffuse form, the lesions occur only focally and not diffusely. They are usually met with as an accessory finding associated with some other condition causing death. Fahr has pointed out that anatomically it might be difficult to differentiate a focal glomerulonephritis from a beginning or healing acute diffuse glomerulonephritis. The same author has called attention to the absence of red cells in the glomerular loops as an indication of a still active nephritis, while the presence of blood here might indicate a subsiding nephritis.

Chronic Focal Glomerulonephritis.—These cases in their onset and course resemble very closely the chronic diffuse glomerulonephritis without kidney insufficiency; many cases are latent, others present pain in the lumbar region, and others may be associated with nephrosis, presenting more or less severe edema. The hematuria without increased blood-pressure and without heart hypertrophy is again the differentiating characteristic. The kidney function is usually unimpaired.

Septic-Interstitial Nephritis.—This occurs almost exclusively as a result of acute streptococcic sepsis, as after scarlet fever, diphtheria, necrotizing angina and wound infections. The indications from the symptoms, physical findings, laboratory and special examinations are usually lacking.

PATHOLOGY.—Macroscopically these kidneys do not present a characteristic appearance. If the microscopical changes are slight, the kidney does not vary from the normal appearance macroscopically. If, however, the interstitial infiltration is marked, the kidney may be swollen, moist, as the result of serous infiltration, and soft in consistency. The cortex and pyramidal substance are well differentiated and the markings of the cortex are indistinct. The macroscopical appearance may indeed be so characteristic as to render a diagnosis possible,—brownish hemorrhagic streaks in the cortex corresponding to brownish flecking on the outer surface, enlargement of the kidney, differentiation of cortex and pyramids (Aschoff).

Microscopically, in mild cases there are small foci of round cell infiltration distributed in the interstitium of the cortex. These foci consists chiefly of lymphocytes and plasma-cells; these areas of infiltration may be between the tubules, separating them and by pressure may destroy them. The glomeruli withstand the destructive process much longer than the tubules, though coagulated masses may be present in the intracapsular space. The capillary loops in the beginning of the process are well filled with blood, but later the blood there is considerably diminished.

Hemorrhage may be present in the larger areas which are found by preference in the boundary zone. When the areas of infiltration reach considerable size they may be seen as boat-shaped areas with base directed towards the outer surface. Other areas of the parenchyma may be intact. The vessels and heart are not changed from the normal. It is questionable whether these kidneys develop into the primary contracted kidney; Aschoff thinks that they may rarely do so.

Embolic Focal Nephritis.—This form of nephritis is usually associated with infectious endocarditis due to the Streptococcus viridans. The symptoms and findings referable to the kidneys are obscured by those due to the infective endocarditis. They may, however, resemble those found in focal glomerulonephritis. These cases are, however, more dence. The degeneration of the tubules is probably largely due to the destruction of the glomeruli to which they belong, but there is evidence that this may in part be due to the direct action of toxins. This process is, however, never so marked or diffuse as in nephrosis. *The connective tissue* is much less uniform than in the second stage. There are quite marked changes in the *blood-vessels*—hyperplastic intimal thickening as well as regressive changes.

How this is brought about is a debated question. There is regularly hypertrophy of the heart, but this does not reach the extent which is seen in the primary contracted kidney. Fahr summarizes his views on these questions in the following way: In glomerulonephritis, especially in the chronic form, the vascular system is under marked strain as a result of the glomerular change accompanied by progressive destruction; this marked strain is the cause of the atherosclerosis of the kidney vessels and the atherosclerosis of the kidney vessels produces an increase of blood-pressure which is added to the primary hypertension produced by the glomerular changes.

ILLUSTRATIVE CASE No. I.—C. P., colored, female, age 26, no occupation. Admitted to Memphis General Hospital, September 10, 1919. Discharged November 4, 1920.

Chief Complaint.—Shortness of breath, swelling of feet and legs, anorexia, matutinal vomiting, pain in the lower abdomen, pollakiuria and nycturia.

Family History.—Father and mother dead, cause unknown; 5 sibs, 1 alive and well, 4 dead, cause unknown; no cancer, tuberculosis, syphilis or nervous disease in family.

Past History.—Has had the usual diseases of childhood; a leukorrheal discharge for about one month.

Menstrual History.—Began at 14; has always been regular, of 28-day type, duration from 3 to 4 days.

Present Illness.—Began three months ago with shortness of breath on exercise. She noticed swelling of the feet and legs two months ago; during this time she has had a poor appetite, attacks of vomiting in the morning and pain in the lower abdomen. The patient states that she has had to urinate every 20 or 30 minutes.

Physical Examination on Admission.—Well-nourished and developed female. Facies shows anxious, distressed expression; fairly marked dyspnea; conjunctivæ pale; tongue, central grayish coating, margins furrowed; moderate edema of the face, especially of the eyelids; notable pallor of oral mucous membranes; teeth in good condition, moderate retraction of gums; pupils react to light. *Thorax:* Expansion poor, respiration largely of abdominal type; apex impulse felt most distinctly in the sixth interspace 2.5 cm. (1 in.) outside the midclavicular line; to the right the area of cardiac dulness extends 2 cm. to the right of the right sternal margin and to the left to the anterior axillary line; there is marked accentuation of both aortic and pulmonic second sounds; there is a gallop rhythm; no murmurs are heard. The liver is apparently within normal limits, the spleen is not felt, there is no sign of free fluid in the abdominal cavity. There is edema of the lower extremities. Temperature 99° F. (37.22° C.). Pulse 102. Blood pressure 175–130.

Urine.—Clear, straw-colored, specific gravity, 1007; reaction neutral. Albumin +; hyalin and granular casts + +; pus cells +. Blood, secondary anemia with slight leukocytosis.

Course.—September 13, 1919, patient had two convulsions—one at 2 P. M. and one at 9:15 P. M. They lasted two or three minutes and patient was in a semi-comatose condition for about 15 minutes following each convulsion. During convulsion pupils were slightly dilated and reacted to light, the breathing was stertorous, there was foaming at the mouth from which some blood exuded, probably due to biting tongue; the patient's attention could be attracted by calling her name, but she would not answer questions.

September 14, 1919, patient had three convulsions to-day.

September 25, 1919, patient's condition has improved considerably the last few days; edema has largely disappeared. She complains of no discomfort except nausea due to taking milk. The heart shows gallop rhythm, aortic second sharply accentuated, bell-like quality; lungs are negative.

September 26, 1919, patient feels better; swelling in feet has almost disappeared.

October 1, 1919, patient is in a stuporous condition, breathing heavily.

October 9, 1919, patient sleeps most of the time during the day.

October 14, 1919, patient complains of pain over precordium, her general condition is growing worse, is stuporous, there is a pericardial friction rub and gallop rhythm.

October 15, 1919, over the entire precordium, there is a pericardial friction rub.

October 16, 1919, patient complains of pain over precordium.

October 17, 1919, feet and legs are more edematous, dyspnea increased.

October 18, 1919, patient complains of pains in the legs and much dyspnea.

October 22, 1919, patient not so well; complains of pains in the epigastrium.

October 27, 1919, pericardial friction now much more pronounced, general edema is more marked, especially in the thighs; patient complains of pain in the right side; she seems very uncomfortable.

October 28, 1919, gallop rhythm, arhythmia and pericardial friction rub very pronounced; edema of extremities more marked; patient is stuporous.

October 29, 1919, patient complains of pains over precordium; asthenia very marked.

October 31, 1919, patient is much worse; semi-delirious; respiration Cheyne-Stokes; pulmonic second sound weak.

likely to be complicated by the picture of nephrosis on the one hand and by insufficiency on the other as shown in an inability to concentrate with hyposthenuria.

PATHOLOGY.—*Macroscopical.*—The kidney is not enlarged, is of firm consistency and very rich in blood. The outer surface and cortex are brownish, and the pyramids dark brown. The cortex and medulla are well differentiated and the cortical markings are distinct. Hemorrhages are not recognizable macroscopically.

Microscopical.—Many of the glomeruli contain emboli of bacteria, usually the Streptococcus viridans, but other organisms have been found. These emboli produce necrosis of a part or the whole of the glomerulus. In the early stages the bacteria, as well as degenerated cells, fibrin and red blood-cells may be demonstrated. The inflammatory reaction around the necrotic areas is usually slight. If the emboli are situated in the peripheral-lying loops, there may be seen a pericapsular leukocytic infiltration. Bowman's capsules are generally empty, but coagulated masses and red blood-cells may be present. If the vasæ efferentiæ are blocked by emboli, the reaction may be so great as to produce miliary abscesses.

The proximal convoluted tubules may show granular degeneration. The tubules may be destroyed; in older cases the necrosis of the glomeruli is replaced by scar tissue. The interstitial tissue is also increased in this stage and as a result of the destroyed glomeruli, the tubules belonging to them show granular degeneration.

THE SCLEROSES

Introduction.—Chronic hypertensive states have been the subject of much confusion with respect to etiology, clinical manifestations and the underlying pathology. For a long time they were all grouped under the term chronic interstitial nephritis, represented by the primary contracted kidney. About 1876 Mahommed introduced the term "the prealbuminuric stage of Bright's disease" by which he would indicate, that there was a period, longer or shorter, of augmented blood-pressure, a period during which the encroachment of the disease could be foretold and perhaps forestalled. At about this time Von Basch began to write of "Latent Arteriosclerosis" and Huchard of "Presclerosis," both indicating that rising pressures often preceded anatomical changes in the kidneys but were due to arteriosclerosis latent or manifest in some part of the body, and did not necessarily represent the incipient stage of renal disease in the ordinary sense.

Also about this time Sir Clifford Allbutt began to elucidate his ideas on this condition and developed a clinical concept to which he gave the name hyperpiesis, believing that the hypertension was due to functional hypertonus of the arterioles, but that arteriosclerosis might develop later as the result of the hypertension. Janeway designated a similar condition as hypertensive cardiovascular disease. By this time the pathologists (Jores, Gaskell, Fahr and others) had shown that the kidney, represented by the term chronic interstitial kidney, primary contracted kidney, did not develop from an inflammatory process at all, but was the result of arteriosclerotic processes affecting the small and smallest blood-vessels of the kidney. In 1914 Volhard and Fahr published their observations made together in a monograph "Die Brightsche Nieren Krankheit." They designated benign hypertension as a clinical condition in which there could be found no evidence of impaired kidney function and represented by kidneys showing pure arteriosclerosis of the small and smallest blood-vessels; macroscopically the kidney may be contracted or noncontracted, while the malignant or combination form was a condition showing impaired kidney function and represented by kidneys which showed in addition to marked arteriosclerotic changes, also changes of an inflammatory or degenerative kind.

Recently Barker has divided the chronic hypertensive states into four groups clinically: (1) Incipient arterial hypertension often accidentally discovered; (2) relatively early chronic arterial hypertension without obvious signs of renal or arterial disease (so-called hyperpiesia, essential hypertension, idiopathic hypertension, etc.); (3) the more advanced stage of chronic arterial hypertension, but before the appearance of serious complications; and (4) late stages of chronic arterial hypertension, with serious complications (cerebral, cardiac, renal, etc.). This author would seem to regard these groups as different stages of the same process. "If patients in whom the diagnosis of so-called primary, or essential hypertension has been made and in whom the disease process has not been arrested at a relatively early stage by treatment, be followed long enough, they will, I venture to say, be found sooner or later to suffer from the same kinds of accidents, and will ultimately make their lethal exitus by the same routes (cerebral apoplexy, myocardial insufficiency, uremic poisoning, or terminal infection) as are characteristic of the histories of patients in whom a diagnosis of arteriosclerotic hypertension, or of nephropathic hypertension, has been made."

The author believes that at the present it is better to distinguish with Volhard and Fahr two groups of scleroses: (1) Benign hypertension, and (2) malignant hypertension (the combination form).

BENIGN HYPERTENSION

(Essential Hypertension, Hyperpiesis, Hypertensive Cardiovascular Disease, Red Granular Kidney, Genuine Contracted Kidney, The Large Smooth Kidney with Diffuse Presclerosis or Arteriosclerosis of the Kidney Vessels)

Etiology.—The etiology of benign hypertension is as obscure as that of arteriosclerosis in general; but all those factors which favor the occurrence of the latter also favor the development of nephrosclerosis.

AGE AND SEX.—In 268 cases of benign hypertension, Volhard and Fahr found that the greatest number occur in the fifth and sixth decades; and that men are possibly more frequently affected than women.

The following table including Volhard and Fahr's cases and 100 of the author's will show the age and sex distribution:

		Volhard and Fahr's Cases			Author's Cases		
Age	Period	Male	Female	Total	Male	Female	Total
To	-20	....	1 (.4%)	1 (.4%)	....	....	....
21	-30	2 (.8%)	....	2 (.8%)	3%	....	3%
31	-40	8 (3.2%)	7 (3%)	15 (6.2%)	3%	3%	6%
41	-50	31 (11.5%)	15 (6.5)	46 (18)	11%	19%	30%
51	-60	48 (14)	34 (16)	82 (30)	25%	13%	38%
61	-70	42 (15.5)	40 (14.5)	82 (30)	12%	5%	17%
71	-80	18 (7%)	19 (7%)	37 (14)	3%	1%	4%
81	-90	....	2 (.8%)	2 (.8)	1%	1%	2%
91	-100	....	1 (.4)	1 (.4)	....	....	....
		149	119 (48%)	268	58%	42%	100

In 50 cases Meara found the age distribution as follows: 56 per cent. fell between 45 and 55 years, and 68 per cent. fell between 45 and 60 years.

HEREDITY.—Attention has often been called to the influence of heredity on the vascular system. It has often been noted that different members of the same family show a tendency to hypertension. The stocky build, short, thick neck, red face and tendency to obesity—the *habitus apoplecticus*—is recognized as a family trait. Migraine, a notoriously hereditary affection, is frequently associated with hypertension.

Familial thyreopathies also predispose to hypertension. Osler used to emphasize the fact that one may start life with different kinds of tubing. Barker has recently added that "this tubing, the vasomotor nervous system innervating it, and the organs of chemical regulation in the body that yield chemical substances that impinge upon both, depend largely upon the source from which the person springs—that is, upon family stock." In 100 cases of benign hypertension there appears in the family history a record of Bright's disease 4 times, of arteriosclerosis 1 time, of paralysis 12 times, of apoplexy 5 times, of heart disease 12 times, of kidney trouble 1 time, and of diabetes 1 time.

WEAR AND TEAR.—Benign hypertension is frequently found in persons who hurry and worry. Its subjects are often found in the upper classes of society, who occupy responsible positions with their necessary mental strain. Physical strain is also an important factor, but not so much so as the former as shown by the fact that only 15 of the 100 cases occurred in a general city hospital as compared with 85 cases in private consultation practice over the same period of time. The series is represented by a great variety of occupations, laborers, housewives, schoolteachers, planters, merchants, insurance men, ministers, college presidents, lawyers, physicians, bankers, real estate men, cotton brokers, sheriffs, horse trainers, clerks, contractors, theater managers, etc. The wear and tear attendant upon any of these callings and the effects of the same are possibly due to the make-up of the individual.

INFECTIONS.—Infections of various kinds also appear in the record of the past history of this series. But it is difficult to estimate with any degree of accuracy the influence of these upon benign hypertension. They as other series show the relative infrequency of syphilis in the record. While Wassermann's were made on each case of the series, it was positive in only five of the one hundred cases.

INTOXICATIONS.—Various intoxications either of an exogenous or endogenous nature have been accredited as causes of atherosclerosis of the kidney vessels. Among the former are alcohol, tobacco, coffee, tea, lead, mercury and zinc; among the latter are the various poisons arising in the gastro-intestinal tract.

The influence of alcohol and tobacco, as well as tea and coffee, is difficult to estimate. It is pointed out by Volhard and Fahr that the Munich-beer heart and the so-called idiopathic cardiac hypertrophy might depend upon hypertonic kidney sclerosis, although the autopsy report on the kidneys in these cases is normal—the kidney sclerosis being overlooked, if careful microscopic examination, including special methods of staining are not carried out.

The general opinion is, however, that alcohol is not a marked factor in the production of kidney sclerosis. The views with respect to tobacco are more at variance. The great frequency with which nephrosclerosis occurs in women would discount tobacco as an important factor. The excessive use of tea and coffee may be favorable for its production. The evidence for any of these including the heavy metals, and gastro-intestinal intoxications is not specially noticeable in the author's series.

METABOLIC DISEASES.—Gout, diabetes, obesity, and the tendency to stone formations have been discussed in their relationship to arteriosclerosis of the kidney. In the author's series there were many overweight and 5 in whom marked obesity existed, and also 6 in whom either frank diabetes or a markedly lessened sugar tolerance existed.

Symptomatology.—The onset of benign hypertension may be quite gradual, indeed a high blood-pressure may exist for several years without producing any symptoms, and be discovered accidently as in the routine examination for life insurance or other cause. Occasionally a cerebral apoplexy may be its first manifestation, or there may be mild symptoms on the part of the arterial system, *e.g.*, nosebleed, flushes of heat, and throbbing in the ears.

However, the symptoms of which the patients usually complain first are those referable to the heart; *i.e.*, hypertension usually makes itself manifest by symptoms when the left heart begins to fail to empty itself against the increased peripheral resistance. Indeed, the cardiac symptoms stand in the foreground throughout the clinical course of the disease.

At first these are the symptoms of relative myocardial insufficiency, which, together with their pathologic physiology, has been discussed under the circulatory nephropathies. There is shortness of breath on exercise, sometimes associated with palpitation. There may be a sense of pressure beneath the sternum, or a sense of constriction in the chest after a heavy meal or excess *in Baccho.* Disturbances of sleep are quite common. The patient cannot lie on his left side on account of the throbbing of the pulses in his ears, which keeps him from going to sleep. The sleep may be restless, disturbed by dreams and nightmares. Frequently the patient awakens suddenly with a start. Attacks of difficult breathing, closely simulating bronchial asthma, are likely to occur especially at night. There may be swelling of the ankles and lower limbs, occurring during the day to disappear after a night's rest.

These attacks of relatively myocardial insufficiency have quite distinct characteristics in benign hypertension. They are borne over a long period of time, and sometimes disappear without any special treatment, and the objective manifestations of myocardial insufficiency may be absent also for a long time.

There is frequently a history of a repetition of these attacks after disappearance, before finally the manifestations of complete cardiac decompensation set in; at this time there is dyspnea even while the patient is at rest, stasis bronchitis takes the place of the paroxysmal attacks of dyspnea, and there is cough with expectoration, arhythmias, digestive disturbances and symptoms of stasis in other organs.

RENAL SYMPTOMS.—These are not prominent in benign hypertension. The patient may complain of nycturia and there may be a slight night polyuria. This is, however, not to be confused with the nycturic polyuria of kidney insufficiency; that of cardiac origin is usually associated with a day oliguria in contradistinction to that of nephritic origin which is usually associated with a day polyuria.

Increased thirst as in chronic diffuse glomerulonephritis in the end stage is not present in benign hypertension with well-compensated heart, but may be present with decompensation. The symptoms with reference to the arterial system are quite numerous and varied. These have been discussed in connection with eclamptic equivalents in the section on Uremia.

As stated above, not infrequently apoplexies occur, as well as mental disturbances, such as progressive dementia and insanity and transitory paralysis as the result of focal cerebral softening from thrombotic processes. More frequent, however, and more prominent are those symptoms due to functional disturbance produced by arteriosclerosis of the cerebral vessels. Headaches, frequently of the type of migraine, dizziness and fainting spells occur. Transitory aphasia, amaurosis, deafness, paralyses, maniacal conditions and epileptiform attacks may also be present. Cheyne-Stokes' breathing is possibly also an arterial symptom often met with. Severe attacks of distressed tachypnea without the presence of physical signs in the chest, which Pal has designated cerebral high tension tachypnea, sometimes occur. The relief afforded these by lumbar puncture would indicate that they are caused by increased intracerebral pressure. Hemorrhages from various sources, nosebleed often difficult to stop, and hematuria are also met with among the arterial symptoms. Recently one of the author's patients had hemoptyses, for which no other cause than the hypertension, which was quite marked, could be discovered.

Hemorrhages may also occur in the subcutaneous tissues as the result of slight traumata. Attacks of angina pectoris and angiospastic symptoms in other areas as angina abdominalis, intermittent claudication and "dead fingers and toes" are not infrequently met with.

Physical Findings.—*General Appearance.*—These patients often appear as if in robust health, the complexion is ruddy, the habitus is plethoric, they are active and frequently are overweight, with a tendency to obesity, though thin people may also be the subject of benign hypertension.

The Blood-pressure.—Increased blood-pressure is one of the pathognomonic signs of benign hypertension. There is some difference of opinion as to just what constitutes an increased pressure. The normal pressure varies according to age. The general average for the different ages may be stated as follows:

15–30	123
30–40	126
40–50	128
50–60	133
60–70	138

These figures as the result of various physiological conditions, such as time of day, sleep, posture, eating, exercise, emotional states, menstruation,may vary 19 or 20 points up or down. The diastolic pressure is normally below the 100 mm. Hg., usually in grown persons from 70 to 80. It is much more constant under various physiological conditions than the systolic pressure—rarely varying more than 6 or 8 points.

In 268 cases of benign hypertension, Volhard and Fahr found values above 200 in 40 per cent., between 170 and 200 in 40 per cent., and below 170 in 20 per cent. In the author's cases, there were values above 200 in 13 per cent., between 170 and 200 in 48 per cent., and from 150 to 170 in 39 per cent.

In the greater number of cases the hypertension is maintained at a more or less constant level, but under certain conditions the systolic pressure may vary up or down—down in early cases as the result of treatment. Often also with the onset of cardiac decompensation the systolic pressure may fall and the diastolic rise. More rarely is there a variation upward, which Pal designates as crises and these rises are usually associated with alarming symptoms of a cardiac or cerebral nature.

The Heart.—As a result of hypertension the heart is regularly enlarged. The hypertrophy at first involves the left ventricle, which it may be difficult to demonstrate at the time by physical signs. By the time relative myocardial insufficiency has been established, the apex beat will be displaced downward and outward and show a heaving character. The area of cardiac dulness will be increased to the left, and often early, but more often later in the disease, the supracardiac area of dulness will be widened as the result of dilatation of the aorta. The aortic second sound is markedly accentuated, as is also the first sound at the apex. There is frequently a presystolic gallop rhythm. In this stage the pulse is usually regular, but may be a little quickened. The hypertrophy will now often be better shown by x-ray examination, which reveals the so-called sock heart, which is due to the hypertrophied left ventricle. The electrocardiogram will show left ventricular preponderance. With the onset of complete cardiac decompensation right ventricular hypertrophy and dilatation will be added to the left ventricular hypertrophy and the area of cardiac dulness will be increased to the right and to the left. The enlargement often is such as to deserve the name *cor bovinum.*

The presystolic gallop rhythm may be replaced by a protodiastolic rhythm. There may be seen sometimes a postsystolic retraction of the chest wall in the apex region and a diastolic shock felt. Possibly as a result of the brusque filling of the flaccid, incompletely emptied ventricle from the increased pressure in the left auricle, an indistinct third heart sound may be heard. Not infrequently the systolic mitral murmur of relative myocardial insufficiency may be heard. The orthodiagram shows all of the diameters of the heart enlarged.

On an average the median right equals 4.6 cm.; the median left 11.3; and the longitudinal 17.5. Arhythmias are now quite frequently present, the most common irregularity being premature contractions. Pulsus alterans is discovered in taking the blood-pressure much oftener than it was formerly supposed to occur. The various stages of heart-block may be observed, and complete disassociation of the auricular and ventricular rhythm is sometimes seen. Auricular fibrillation is not usually seen until the late stages of myocardial insufficiency or unless the benign hypertension is associated with mitral stenosis.

Valvular diseases are not infrequently associated with benign hypertension. The one most often met with is aortic regurgitation, which may arise on an arteriosclerotic or leutic basis. Occasionally also aortic stenosis or mitral stenosis may occur on an arteriosclerotic basis.

An abnormal presystolic pulsation and swelling of the veins of the neck may be made out. The liver is enlarged and may be felt to pulsate. The venous pressure is markedly increased. Under certain conditions such as very advanced age, emaciation, weakening disease and prolonged enforced rest, and disturbances in the blood supply to the heart muscle by sclerosis of the coronary arteries, cardiac hypertrophy may be absent, or slight.

Edema.—This is lacking in the compensated stages of hypertension. In the stage of decompensation it is frequent and may reach extreme grades.

Laboratory Examinations.—*Urine.*—This may be entirely normal as to color, quantity, specific gravity, albumin and casts for a long time.

Frequently, however, a trace of albumin and a few casts may be present. With the onset of myocardial insufficiency it may show the characteristics of the stasis kidney,—oliguria, high fixed specific gravity, albumin, casts, leukocytes and red blood-cells. With the elimination of edema there may be polyuria with low specific gravity (see *Circulatory Nephropathies*).

Blood.—There is usually no evidence of anemia; on the contrary, there is more frequently a moderate polycythemia which is in marked contrast to the blood findings in the end stage of diffuse glomerulonephritis and the combination form.

Special Examinations.—*Ophthalmoscopic.*—Eye-ground examinations are of great diagnostic value. It is sometimes the only evidence as to whether a given case is to be regarded as benign or malignant hypertension. In the greater number of cases of benign hypertension the eye-grounds are normal; frequently, however, the retinal arteries will appear contracted and tortuous with thickened walls. The veins will be widened. Due to arteriosclerosis, small hemorrhages and areas of degeneration may be present, but the characteristic changes of albuminuric retinitis do not occur.

Kidney Functional Tests.—The second pathognomonic finding in benign hypertension is the absence, as a rule, of impaired functional capacity of the kidney, as determined by the usual functional tests.

According to Volhard, there are three groups of cases with respect to the water test. In the first group which contains the greatest number of cases, 1500 c.c. of water taken on a fasting stomach is excreted in four hours and the greater part in the first two hours with lowering of the specific gravity, *i.e.*, as in health.

In the second group, which includes quite a number of cases, the test is excessive, *i.e.*, more than 1500 c.c. are excreted in four hours. This is likely to occur in cases which show transitory hypertension, *i.e.*, in cases which under treatment show a tendency to a falling of the blood-pressure. The third group shows a poor result, *i.e.*, less than 1500 c.c. are excreted in four hours or the total quantity is excreted over a much prolonged time. This is especially likely to occur in cases with marked cardiac decompensation and in cases which have been on a dry diet for a long time because a greater part of the water taken in is retained by the thirsty tissues.

Concentration Test.—On an absolutely dry diet, the specific gravity of urine rises regularly as in health. It may reach 1025 or 1030 after 8 to 12 hours. This test is difficult to carry out in cases associated with cardiac decompensation. In the latter cases the ability of the kidney to excrete water, salt and nitrogen is the same as in the stasis kidney (*q.v.*).

Phenolsulphonephthalein Test.—In compensated cases the phthalein output is normal, *i.e.*, 50 per cent. or more in two hours and 10 minutes. In cases with myocardial insufficiency the output may be low and return to normal upon the restoration of compensation.

Meara reports the following findings with respect to this test:

Cases Observed	*Phthalein Output in 2 hrs.*
5	70–80%
11	60–70%
8	50–60%
6	30–40%
1	5%

Retention Tests.—Meara found the following values as to uric acid, urea nitrogen, non-protein nitrogen and creatinin in hyperpiesia:

Uric acid in the blood (43 cases); 44 per cent. showed some retention and 56 per cent. normal values.

Urea Nitrogen (42 cases); taking 20 mg. or less per 100 c.c. as normal, 20 to 25 mg. per 100 c.c. as debatable, 77.6 per cent. showed normal values and 21.6 per cent. frank retention, but in only 4 did the values run above 30 mg. and the highest of these was 48 mg.

Non-protein Nitrogen (12 cases); there were 35 mg. per 100 c.c. or less in 3 cases; from 35 to 45 mg. in 6 cases; 45 to 50 mg. in 2 cases; and 78 mg. in 1 case.

Creatinin (16 cases); 11 cases showed 3 mg. per 100 c.c. or less; 4 cases 3 to 4 mg.; 1 case 4 to 8 mg.(3 mg. or less is taken as normal).

Volhard and Fahr made non-protein nitrogen estimations in the blood fifty-eight times in benign hypertension and found values varying within normal limits, *i.e.*, up to 50 mg. per 100 c.c. They state that in cases of severe cardiac insufficiency, shortly before death and in cases in which edema is being eliminated somewhat higher values were found.

In the author's cases the modified Mosenthal test has been normal or shown the characteristics of the stasis kidney. The phthalein test was within normal limits in compensated cases, but may be markedly lowered in severe myocardial insufficiency. *The blood urea* has been within normal limits. In compensated cases there have been from 19.5 mg. to 50 mg. per 100 c.c. of blood.

The average of 55 cases was 34.7 mg. per 100 c.c. In severe decompensation and during the elimination of edema the upper limits of normal (50 mg. per 100 c.c.) has been usual, one time rising to 62 mg. per 100 c.c.

Basal Metabolism.—According to Mosenthal and Marks, the basal metabolic rate in cardiorenal disease without dyspnea is normal + 10; in cases with dyspnea it is from + 25 to + 50. Barker states that some of the hypertensions have an increased rate, some a decreased rate and many a normal rate.

Diagnostic Features.—(1) It usually occurs after the fiftieth year of life and is of quite frequent occurrence.

(2) It begins and runs its course as a cardiovascular disease. If a cerebral vascular accident is not the first manifestation, the first symptoms begin to make themselves noticeable when the left ventricle begins to weaken as it is no longer able to empty itself against the increased resistance. The symptoms are those of relative myocardial insufficiency, and the patient oscillates a long time between compensation and complete decompensation. Finally the latter sets in with its usual symptoms.

As a result of the association of arteriosclerosis in other areas in those patients of rather advanced age, arterial symptoms form a prominent part of the clinical history.

(3) The general condition is good. "These patients are usually of ruddy complexion, stocky build, plethoric habits, active temperament, live men and women" (Meara). Still, here, exceptions may occur.

(4) There is high blood-pressure; at first these may consist of transitory rises.

(5) The heart is markedly hypertrophied, at first involving chiefly the left ventricle, when it may be difficult of demonstration by physical signs, although teleoroentgenograms or orthodiagrams always show the hypertrophy of the so-called sock heart. With the onset of decompensation dilatation sets in with enlargement of the heart to the right and left.

(6) The blood rarely ever shows an anemia; indeed there is frequently a marked polycythemia—a valuable distinction from the end stage of chronic diffuse glomerulonephritis and the combination form.

(7) The urine often shows no abnormality at all, not infrequently a trace of albumin and a few casts; often there is nycturia and a moderate night polyuria, the cardiac origin of which is readily recognized by the accompanying day oliguria.

(8) The eye-ground changes are those of arteriosclerosis, never those of chronic nephritis. The presence of papillitis and neuroretinitis is conclusive evidence that the case has passed into the combination form.

(9) The kidney function is unimpaired. It excretes water as usual. It concentrates normally; phthalein excretion is good; there is no increase in the blood urea and non-protein nitrogen. There are conflicting views with respect to salt excretion which need further study.

(10) The form of uremia, so called, which is characteristic of this form of disease is that in which eclamptic equivalents occur, such symptom as headaches, dizziness, Cheyne-Stokes' respiration, nocturnal asthma, cerebral crises, transitory aphasia and paralysis, increased reflexes, physical disturbances, etc. Eclamptic uremia may rarely occur, true uremia with azotemia is regularly absent.

Treatment.—So little is known of the real cause and pathogenesis of arteriosclerosis of the small and smallest blood-vessels of the kidney that but little can be done in the way of prophylaxis. Especially those who are hereditarily disposed should avoid strain both physical and mental and should guard against infection, endogenous and exogenous intoxications and metabolic diseases.

In the management of benign hypertension it is well to realize what may be accomplished in the way of treatment—that the early cases may be cured, the more advanced arrested and many of the severe symptoms in the late stages palliated. These results may be accomplished by the judicious application of psycotherapy; regulation of the diet; sane advice as to work, rest, exercise and vacation; the careful use of hydro-, mechanico- and electrotherapy; the proper use of drugs; control of infections; and the application of certain surgical procedures.

PSYCHOTHERAPY.—It is desirable to dispel fear where this can honestly be done; it is absolutely necessary to inspire the patient with confidence and hope; and he should be encouraged to lead a hygienic life and cultivate equanimity. To accomplish these things it is necessary to know the minutest details of the patient's habits, to make a most careful investigation of the case, to impress upon him the nature of the illness, to convince him that he will have the doctor's best efforts to do the best thing for him, and to set him right on the significance of a high blood-pressure. He should be made to realize that with care and perseverance the early case can be cured. He may have to change entirely his mode of life, but the results obtained will make this worth while. Even in an advanced case he may be kept in functional activity of both body and mind and even in the last stages much may be done in the way of palliation.

He must be taught that the dangers of the disease are to be expected, chiefly from the failure of the heart and a vascular accident, that the high blood-pressure is a compensatory process to meet the demands made on the cardiovascular system and needs not to be treated as such. Only if danger of apoplexy or hemorrhage into other important organs threaten should especial measures be instituted to reduce it.

DIET.—As there is no impairment of the kidney function, no especial restriction as to the proteins is necessary. It must ever be kept in mind that the patient's nutrition must be maintained and an effort made to give such quantity of food as will keep his weight just below his ideal, calculated standard. The proper balance of diet must be considered. In a general way, the patient may be advised to let his diet consist chiefly of bread, milk and vegetables, with a small piece of meat once a day. He should especially avoid large quantities of meat, meat broths, spices, alcohols, acids and an excessive quantity of salt. Due consideration should be given to the patient's tastes and power of digestion.

The motto of the hypertonic should be "To avoid hurry and worry." Both physical and mental strain in this condition predispose to the development of cardiac insufficiency and cerebral hemorrhage. In the early stages of the disease the patient's occupation need not be given up. If, however, it has entailed great haste and worry, the patient must be urged to slow down. Shorten the hours of work, take more vacations, indulge in pleasant recreation, not forgetting, however, that in the latter, excesses may easily be reached. Good advice for these patients is that any exercise which produces undue shortness of breath is too much.

HYDRO-, MECHANICO-, AND ELECTROTHERAPY.—The author has obtained the impression that these forms of therapy are often overdone with hypertonic patients. In the first stages of the disease the bathing habits may be those of an ordinary healthy person. In the later stages, the baths should be neither hot nor cold, but warm or tepid. Here especially should violent forms of hydrotherapy and mechanicotherapy be avoided. A yearly visit to a Spa where these forms of treatment are not carried to excess is often beneficial. Massage may be of advantage in those cases where periods of enforced rest are necessary.

The application of high frequency currents in cases of benign hypertension has been highly praised by some, but the author's impression from observation is that they, as other forms of electrotherapeutics, have little value other than that of a psychic nature.

While it is true that a dry, equable climate is best suited for the hypertensive patients, it is possible by protection—proper clothing, the avoidance of chilling and exposure to inclement weather—to get along very well in any place in which circumstances may place one.

Drugs have a place in the treatment of benign hypertension. If constipation exists, an effort should be made to overcome this by diet, exercise, and habits, and when necessary, **mineral oil** and a **gentle laxative** may be given by night, supplemented by **mild salines** in the morning. In any event a dose of **blue mass** combined with **euonymin** and **extract of Hyoscyamus** (masse Hydrargyrii, grains 10 [.65 gram], euonymin, grains 3 [.195 gram], extractum Hyoscyami, grain ½ [.0324 gram], in capsule) may be taken at bed time once every week or two with advantage.

Small doses of **iodids** over a long period of time with regular interruptions may be of advantage, but it should not be forgotten that patients who have a tendency to hyperthyroidism, emaciation and severe headaches do not bear iodids well. They should not, of course, be used in those patients who present a special idiosyncrasy against them. The vasodilators—**nitrites, nitroglycerin, erythrol tetranitrate**—are of but little advantage except in those cases associated with angina pectoris or threatened cerebral apoplexy.

In the early and moderately advanced stages of benign hypertension all definite foci of infection, as in the tonsils, paranasal sinuses, teeth, chronic cholecystitis, chronic appendicitis, chronic prostatitis should receive the appropriate surgical treatment. In the later stages, however, great care should be exercised not to subject the patient to unnecessary surgical procedures, or to such as may result more seriously to the patient than the condition for which they are undertaken.

Such complications as myocardial insufficiency and eclamptic equivalents have been fully discussed in the sections on circulatory nephropathies and uremia (*q.v.*).

In cases complicated by angina pectoris, those things which are found to bring on the pain—exercise, indiscretions in diet, tobacco, etc.,—should be avoided and nitroglycerin or the nitrites administered both during the attack and in the intervals.

Complicating infections should receive prompt and appropriate treatment.

Prognosis.—In its early stages benign hypertension is a curable disease. In more advanced stages its progress may be arrested or delayed, while in the most advanced stages many of its symptoms may for a long time be ameliorated.

The dangers are first from the heart, second from the arteries, and third from pulmonary complications. In 86 cases of death from the disease, Volhard and Fahr noted 7 from intercurrent disease, 51 from cardiac insufficiency (10 of which were associated with bronchopneumonia), 18 from cerebral arteriosclerosis (11 softening, 5 hemorrhage, and 2 suicide), 10 from bronchopneumonia and 3 from lobar pneumonia. Not one of these cases resulted in death because of kidney insufficiency.

Pathology.—The Kidney.—*Macroscopical.*—The gross appearance of the kidney varies greatly according to the size of the vessels involved and the extent of the arteriosclerotic process. In 89 cases of Volhard and Fahr which came to autopsy, 37 showed contracted kidneys and 52 noncontracted kidneys. The appearance of the contracted kidney will depend upon the distribution of the arteriosclerosis. If the larger vessels are involved, a more or less unevenness of the kidney will result; if the small vessels, a fine granulation. With diffuse involvement of the smaller vessels, the granulations differ from those in the end stage of chronic diffuse glomerulonephritis. In the latter, the islands of widened and hypertrophied tubules are responsible for the granulation, while in the former the granulations are produced by scarring retractions between which the parenchyma is intact.

The primary contracted kidney is greatly diminished in size, the capsule is adherent, the outer surface is finely granular and red. On cut surface, the cortex markedly thinned and red in color, the cortical markings are preserved and the cortex and pyramids are well differentiated from each other. There is a marked tendency to the formation of small cysts.

In the noncontracted kidneys of benign hypertension, which are apparently of more frequent occurrence, the size is not diminished, but may be enlarged as the result of chronic passive congestion.

It is brownish red in color and the consistency is firm. The cortical markings are preserved and the cortex is differentiated from the pyramids. Many of these kidneys without careful microscopic examination would possibly be reported as normal.

Ziegler's findings with respect to arteriosclerosis have been confirmed by subsequent observers. The arteriosclerosis of the vessels produces disturbances in nutrition which occur focally and lead to degeneration of larger or smaller areas of the kidney. The areas of degeneration are replaced by wedge-shaped areas of connective tissue in which the glomeruli are destroyed. Jores believed that, due to the frequent involvement of the vasa afferentia, the glomerulus is destroyed as a whole. Fahr, however, states that by serial sections, the various steps of the destruction may be seen and that a part of the capillary loops may be destroyed. Those tubules belonging to the destroyed glomeruli also undergo destruction. Those which are preserved may contain hyalin casts. The portions of the parenchyma whose blood supply is not involved in the arteriosclerotic process is intact.

The changes in the small vessels consist of hyperplastic intimal thickening which by some is called the stage of presclerosis, and regressive changes which are designated arteriosclerosis.

The heart is regularly hypertrophied and usually reaches an extreme degree. Among 128 cases, Fahr classified the kidneys according to the extent of the vascular changes. In Group I were placed those cases in which all sections showed considerable arteriosclerotic changes not only in the medium and large vessels, but more or less pronounced changes in the small vessels (interlobular and afferentiæ). In Group II were placed such as showed distinct changes in medium-sized vessels, but also found here and there in the small vessels, though much less marked than in Group I.

In Group III changes are completely lacking in the small vessels (afferentiæ and interlobular); in the medium-sized vessels (arciformes and larger branches of the interlobular), hyperplastic intimal thickening with sometimes transition to arteriosclerosis is present, but often slight or completely absent.

In Group I (41 cases) heart hypertrophy was present 34 times. In 13 cases the heart weight exceeded 400 grams (.88 lb.); in 21, the weight was between 300 and 400 grams. Cardiac hypertrophy was absent in seven cases.

In Group II (45 cases), heart hypertrophy was present in 51 cases. In 12, the heart weight exceeded 400 grams; in 19, the weight was between 300 and 400 grams. There was no hypertrophy in 14 cases.

In Group III heart hypertrophy was lacking throughout.

There are different views with respect to the cause of heart hypertrophy and increased blood-pressure in these cases. Two possibilities have been chiefly discussed: (1) arteriosclerosis of the small blood-vessels, especially those of the kidney produce the hypertension and cardiac hypertrophy; (2) some cause, either intra- or extrarenal in origin, tends to produce increased blood-pressure, and this, on the one hand, leads to changes in the small blood-vessels and on the other, to hypertrophy of the heart.

Fahr accepts the mechanical theory, and after discussing the objections raised to this view by Ludwig, Senator and Katzenstein, concludes that the most important cause for the origin of the increased blood-pressure and heart hypertrophy must be sought in the arteriosclerosis of the small vessels. Other organs, especially the pancreas, spleen and brain, may come into consideration, but the arteriosclerotic changes of the small vessels of the kidney occupy the chief place.

Jores states: "For some reason still unknown, the cardiac hypertrophy connected with the primary contracted kidney is more advanced than that associated with any other form of Bright's disease. Investigating this question, I found that the degree of cardiac hypertrophy can depend neither upon the variety nor the severity of the renal lesion; furthermore, the enlargement is present while changes in the kidney are still insignificant. I, therefore, consider it possible, nay, even probable, that in the case of the primary contracted kidney, the heightened blood-pressure is not produced, or at least not solely produced, by the condition in the kidney, but rather by extrarenal causes. This being true, a primarily heightened blood-pressure would have to be regarded as the basic condition responsible for both the cardiac and the renal lesion (Frank), or, as I have expressed it, it would have to be assumed that the noxa which causes the contracted kidney induces, from the first, an augmentation of blood-pressure.''

Among the changes found throughout the remainder of the body in connection with benign hypertension are such consequences of arteriosclerosis as cerebral hemorrhage and necrosis of the myocardium, which supervenes only rarely and as a result of extensive disease in the coronary arteries.

ILLUSTRATIVE CASE No. I.—J. L. M., male, age 44, married, wholesale furniture dealer. Observed November 3, 1920.

Chief Complaint.—Spitting blood for the past two or three days.

Family History.—Father, alive and well; mother, alive and well; 8 sibs, 7 alive and well, 1 dead, cause unknown.

Past History.—Measles, whooping-cough, pneumonia in childhood. Has never been sick since grown. He has been very actively engaged in business for the last twenty years without a vacation. Under great physical and mental strain.

Present Illness.—On the night of November 1, 1920, he felt as if he wanted to expectorate. When he did, he brought up about one teaspoonful of bright red blood. The sputum the next day was streaked with blood. To-day it is clear. The patient has not felt as if he has had any fever; he lost no weight and feels well.

Physical Examination.—The patient's weight is 167 lbs. His average weight is 160 lbs. Temperature 98.2° F. (36.77° C.). Pulse 72, blood-pressure 180–120. The tonsils are enlarged and ragged and he has recently had an abscessed tooth. There is no adenopathy. The chest moves full and equally. There is nowhere any abnormality to palpation, percussion or auscultation. The heart is enlarged, the apex being in the sixth interspace outside the midclavicular line. The rhythm is normal, the sounds are clear and the aortic sound is markedly accentuated. The abdomen and nervous system are without abnormal findings.

The temperature takings at 8, 12, 4, and 8 daily for five days did not show any increase above normal. The blood-pressure on November 6, in the afternoon, was 182–120.

Urine.—Specific gravity 1014; acid, no albumin, no sugar, no casts.

Blood.—Hemoglobin 100 per cent. (Sahli); red cells 5,020,000; leukocytes 8,200; polymorphonuclears 65 per cent.; small lymphocytes 21 per cent.; large mononuclears 11 per cent.; and basophils 3 per cent. Wassermann was negative. Examination of specimen of sputum obtained on four separate days was negative for tubercle bacilli.

Special Examination.—X-ray (stereoscopic plates) shows peribronchial thickening over both lungs, a calcified area in the left lung about the area of the seventh rib. Thickening more marked in the lower lobes. The hili are thickened. There is an area of infiltration at apex of left lung level of the third rib.

Nose and Throat.—The tonsils are infected. There is free blood on the vocal chords; there is no evidence of thickening or ulceration.

Modified Mosenthal.—Ordinary diet with all fluids taken at meal times.

Urine Reaction to Mosenthal Test

Time	Quantity	Specific Gravity	Water	Blood Urea	Creatinin
10 A. M.	78 c.c.	1018			
12 M.	91 c.c.	1016			
2 P. M.	185 c.c.	1010			
4 P. M.	120 c.c.	1010			
6 P. M.	70 c.c.	1018			
8 P. M.	70 c.c.	1020			
Total day	614 c.c.				
Total night	577 c.c.	1016			
Total 24 hrs.	1191 c.c.		1721 c.c.	28.5 mg. per 100 c.c.	1.6 mg. per 100 c.c.

Clinical Diagnosis.—Focal infection tonsils and teeth, hemoptysis slight, and benign hypertension.

Illustrative Case No. II.—Mrs. A. H. M., consulted the author at office, May 18, 1921. Female, 47 years of age, married, housewife.

Chief Complaint.—Periodical attacks of dizziness during which she is unable to stand. Duration 3 months.

Family History.—Father, alive and well; mother, died of Bright's disease; 6 sibs, 5 alive and well; 1 died in infancy.

Past History.—Measles, pertussis, malaria and bronchopneumonia in childhood. Had a nervous breakdown at the age of 22.

Menstrural History.—Menstruation began at 15 years of age. It was always regular, until menopause which occurred 5 years ago. She has had no pregnancies. Married 30 years.

Present Illness.—About five months ago awoke one morning feeling quite dizzy, accompanied by nausea. She took purgatives, but they gave no relief. The attacks have come irregularly since that time, sometimes accompanied by nausea, but not always. The patient remained in bed for two months, but the dizziness was not improved.

She thinks she has lost about 10 pounds in weight during this time. The appetite is variable and occasionally there is a pain radiating along the left costal border. She has become very weak. Symptoms referable to the urinary system are negative. She has no cramping sensations, but is annoyed by a buzzing noise in the ears, particularly the left.

Physical Examinations.—The patient, a lady, is slightly undernourished, 16 lbs. underweight; the skin is subicteric and the mucous membranes are pale. Temperature 99.4° F. (37.44° C.), pulse 124 per minute, blood-pressure, 190–110. The *tongue* is large with indentations in the margin; there is much dental work, mostly fillings; the *teeth* are not sensitive and the gums are in good condition. The *throat* is negative. The posterior cervical glands (left) and submental glands are slightly enlarged. The *thyroid* is barely palpable, not granular nor vascular. The patient is a little hoarse. *Chest:* The respiratory movements are full and equal on both sides. The vocal fremitus is slightly diminished at left apex. The respiratory murmur is clear throughout both sides of the chest. *Heart:* The apex beat is in the sixth interspace outside the midclavicular line, there is marked tachycardia and accentuation of the aortic second sound; the heart is, otherwise, negative. *Abdomen:* No masses or areas of tenderness. It presents the visceroptotic habitus and right kidney is movable (second degree). *Nervous System:* Von Graefe positive; Dalrymple slightly positive; Stellwag negative; Möbius negative; Jellinek positive; Rosenbach positive. There is slight nystagmus on looking upward, none to the right or left. Finger to nose test imperfect. Pass points on the right o.k., two inches to the right on the left side. The deep reflexes are active, the superficial normal. Dermographia is present. There is very slight exophthalmos, and a fine tremor of the outstretched hand.

Laboratory Findings.—Urine.—Light yellow, specific gravity 1010, acid, albumin and sugar negative. Microscopically, epithelium, a few mucous shreds—no casts. *Blood:* Polymorphonuclears 56 per cent.; small lymphocytes 37 per cent.; large mononuclears 5 per cent.; basophils 2 per cent. The red cells are normal in size and in staining reaction. Wassermann, negative. *Gastric Contents:* Dock test breakfast; removed after 45 minutes, 20 c.c., dark brown, a large quantity of mucus. Free blood present, free HCl 8; total acidity 58.

Special Examinations.—Basal metabolism (Jones' Metabolimeter). Age 47; height 61.5 ins.; pulse 126; patient was not excited and breathed quietly; weight 101 lbs.; first liter of oxygen, 5.2 min.; second liter of oxygen, 5 min.; basal metabolic rate—8.

X-ray of Stomach.—Meal 4 ounces of barium; 1st plate, 10 minutes after meal; 2nd plate, 15 minutes after meal; and 3rd plate, 4 hours after meal. The stomach is ptosed, shows no deformities, is well formed. Duodenal caps shows deformity. There is a moderate four-hour residue. Impression duodenal ulcer. *Barany Tests:* Show toxic labyrinthinitis. The left practically destroyed. The blood urea was 31.5 mg. per 100 c.c.

Clinical Diagnosis.—Benign hypertension, toxic labyrinthinitis, and duodenal ulcer.

Treatment.—Sippy régime for duodenal ulcer, the avoidance of hurry and worry. The patient returned September 13, 1921. She feels a great deal better, she says practically well; she has gained 16 lbs., her ideal calculated weight, but is at times still dizzy. The blood-pressure is 200-100, the urine contains neither albumin nor casts and the blood urea is 33 mg. per 100 c.c.

Illustrative Case No. III.—M. G. R. K., male, age 38, married, railroad agent. Seen at office, March 4, 1921.

Chief Complaint.—Paralysis of the right side of the body, February 9, 1921.

Family History.—Father, died of pneumonia; mother, died of apoplexy; one sib, alive and well.

Past History.—Typhoid in childhood; malaria 16 years ago. Tripper and lues denied. Up to several years ago, used alcoholic beverages to excess. Wassermann in July, 1920, was negative.

Present Illness.—On February 9, 1921, while in a fit of anger, the patient felt a burning sensation in the left side of the face, the tongue became thick and the speech was impaired. The left side of the face and the tongue became paralyzed. There was no loss of consciousness. At this time there was a feeling of weakness in the right arm and leg, but he was not completely paralyzed until the next day, *i.e.*, the right arm was completely paralyzed but he was able to move the leg slightly. In about a week the arm began to improve and has gradually improved ever since. He feels very well now.

Physical Examination.—Well-nourished gentleman, 170 lbs., 5 ft., 9½ ins. in height, about 10 lbs. over his calculated ideal weight. Left eye out, result of an injury several years ago. Right pupil dilated, reacts to light. Residual paralysis of the left facial. Teeth, pyorrhea; throat red. Temperature 98° F. (36.66° C.). Pulse 84 per minute. Blood-pressure 190–120. The lungs are negative. The heart is slightly hypertrophied; there is no evidence of decompensation. There is residual paralysis of the right side of the body. Right patellar markedly increased; Babinski positive on the right.

Laboratory Findings.—*Urine.*—Cloudy, yellow, specific gravity 1016; acid in reaction, albumin and sugar negative. Microscopically, a rare red blood-cell is shown; no casts. *Blood:* Polymorphonuclears 67 per cent.; small lymphocytes 37 per cent.; large mononuclears 6 per cent.; red cells, normal as to size, shape and staining reactions. Wassermann—negative. *Kidney Function:* Phthalein 65 per cent. in 2 hours and 10 min. Blood urea 21 mg. per 100 c.c.

Clinical Diagnosis.—Benign hypertension, and crossed hemiplegia.

Illustrative Case No. IV.—Mrs. W. A. S., age 62, married, housewife. Seen first at office, October 31, 1919.

Chief Complaint.—Pain left side of chest for two or three days.

Family History.—Father died of stomach trouble; mother, of gallbladder disease; 7 sibs; one brother died of paralysis; one sister suffers from high blood-pressure.

Past History.—Had typhoid fever in 1896. Pneumonia. Gallbladder diseases, colic, and passed gall-stones 15 years ago.

Marital History.—Five children; menopause 10 years ago.

Present Illness.—About two weeks ago had general aching which was intense. Had been under a severe strain as a result of brother's illness.

A few days ago had an attack of severe pain in the left side with temperature of 101° F. (38.33° C.). The pain was relieved in about three days. Has had no fever since. The throat was sore at this time. The patient still complains of weakness and nervousness. About 4 A. M. Wednesday, she had a collapse, weak and irregular pulse. This was relieved by aromatic spirits of ammonia and hot water. She has had a great deal of cold, clammy perspiration. Has shortness of breath on exercise for the last three years. Her feet swell slightly at times. Her digestion is very good. Gets up several times at night to void bladder. She passes a "large quantity of urine as clear as spring water." She is very nervous—tremor, paresthesias,—and is easily upset.

Physical Examination.—She is well nourished, over weight. Temperature 99° F. (37.22° C.); pulse 96 per minute; blood-pressure 220–120. The teeth are very bad. The throat is red. There is a pleuritic friction rub in the left lower axilla. The heart is hypertrophied. The apex is in the sixth intercostal space outside the midclavicular line. The aortic second is markedly accentuated. The abdomen and nervous systems are without abnormal findings. The urine was clear, specific gravity 1015, albumin present, no sugar; microscopically, an occasional hyalin cast. The blood showed no evidence of anemia. The phenolsulphonephthalein output was 84 per cent. in 2 hours and 10 minutes.

Diagnosis.—Benign hypertension, and fibrinous pleurisy.

Treatment.—The patient was talked to frankly as to her condition, advised to avoid hurry and worry; to let her diet consist chiefly of milk and vegetables with a small piece of meat once a day; to take a mercurial purge once every week or two, etc. She returned July 27, 1920, and went into the hospital for a few days. She had felt much better until recently; she thinks she had taken more exercise and eaten more than she should. Her general condition was about the same. Blood-pressure 210–110. The symptoms of relative myocardial insufficiency had been much better, but recently she had been quite short of breath on exercise.

The patient was kept in bed for two weeks, given an O'Hare diet sheet with a score of 15 for one week, and after that of 20; fluids limited to 1500 c.c. per day. She returned June 20, 1921. Her teeth had been extracted, and she was feeling very well indeed. Temperature normal, pulse 96, blood-pressure 210–130. The apex beat was in the sixth interspace just outside the midclavicular line. There was no evidence of stasis anywhere. *Urine:* Cloudy, yellow, specific gravity, 1016, acid, albumin and sugar negative; microscopically hyalin casts, pus cells + +, and epithelial cells + + +. *Blood:* Red cells 5,250,000; hemoglobin 100 per cent. (Sahli); white cells, 6,500; polymorphonuclears 66 per cent.; small lymphocytes 20 per cent.; large mononuclears 13 per cent.; basophils 1 per cent. *Blood Urea:* 39 mg. per 100 c.c. *Creatinin:* 2.09 mg. per 100 c.c.

Functional Tests.—July 27 to 30, 1920, at rest in bed, on an ordinary diet, with the total intake of fluids at meal times.

Mosenthal Test

Time	Quantity	Specific Gravity	NaCl		Nitrogen	
			Per cent.	Grams	Per cent.	Grams
8–10 A. M.	22 c.c.	1020				
10 A. M.–12 M.	155 c.c.	1015				
12 M.–2 P. M.	90 c.c.	1017				
2–4 P. M.	70 c.c.	1021				
4–6 P. M.	55 c.c.	1025				
6–8 P. M.	65 c.c.	1029				
Total day	457 c.c.		1.08	4.58	.608	2.39
Total night	610 c.c.	1018	1.095	8.82	.546	3.22
Total 24 hrs.	1067 c.c.			13.40		5.61
Intake	1720 c.c. (fluid)			8		13
Phenolsulpho-nephthalein output	15 per cent. in 2 hrs., 10 mins.					
Blood urea	62 mg. per 100 c.c.					
Creatinin	1.9 mg. per 100 c.c.					

The patient returned on October 28, 1921. She had spent the summer on the Gulf Coast and had progressed nicely. At this time her blood-pressure was 200–120. *Urine:* Pale, yellow, specific gravity 1015, acid, albumin—a trace. Sugar—negative. Microscopically no casts. *Blood Urea:* 41 mg. per 100 c.c.

MALIGNANT HYPERTENSION

(*Combination Form of Hypertension, Sclerosis Plus Nephritis, Genuine Contracted Kidney with Tendency to Kidney Insufficiency*)

As many times stated, the malignant form of hypertension includes sclerosis of the small and smallest blood-vessels of the kidney combined with gradual and progressive chronic glomerulonephritis. The sclerosis with complicated acute nephritis is not included.

Etiology.—The etiology of the arteriosclerosis of the kidney vessels is the same, as far as known, as that of benign hypertension. The cause of the superimposed degeneration and inflammatory lesions of the glomeruli is as little known as that of arteriosclerosis. Volhard has discussed two possibilities: (1) That these changes are due to an unknown physiologic product of metabolism which acts toxically on an arteriosclerotic basis; and (2) that they are due to an abnormal path-

Case No.		Erythrocytes	Leukocytes	Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Mast Cell	Wassermann	Eye-grounds	Basal Metabolism	
(1)				56	37	5	2				
(2)	15 Sp. Gr.			66	18	16		N			
(3)	010			67	25	7	1	N			
(4)				61	25	14		N			
(5)				62	35	3		N			
(6)											
(7)	4 cc 1020 Sp. Gr			75	20	5		N			
(8)	-1016 Sp. Gr.			56	38	6		N			
(9				52	40	8		N			
(1								+++			
(1	-1018 Sp Gr.	5¼ M	6.5 m	66	20	13		N			
(1				64	30	6		N			
(1				56	34	10		N			
(1								N			
(1				46	36	16		N			
(1				55	41	3		N			
(1		4 35 M	5 6 m.	54	38	5		N			
(1				67	26	7		N		+40	
(1				71	20	9		N			
(2				69	22	9		N			
(2	.—1010 Sp Gr.							N			
(2				72	24	3	1	++			
(2	1012 Sp Gr.		7.6 m.	70	33	5	2	N			
(2				53	35	12		N			
(2				55	40	4		N			1
(2				77	16	17		++++			8
(2		5.5 M	7.4 m.	71	22	7		N			8
(2				85	6	8	1	N			
(2	1006 Sp. Gr.			63	22	4		N			
(3				62	35	3		N			
(3				77	13	7	2	N			
(3	–1016 Sp. Gr.	5 MB	8.3 m.	65	20	11	3	N			

Case No.	Age	Sex	Weight
(34)	35	F	+++
(35)	51	F	Norm
(36)	52	F	++
(37)	58	M	++
(38)	53	M	+
(39)	82	M	
(40)	76	F	—
(41)	28	F	+
(42)	66	F	
(43)	50	F	++
(44)	55	F	+
(45)	60	M	+9
(46)	48	M	+1
(47)	53	M	++
(48)	50	F	
(49)	62	M	
(50)	67	F	++
(51)	50	F	+
(52)	54	M	++
(53)	50	M	+
(54)	50	M	++
(55)	53	M	++
(56)	57	M	
(57)	57	F	+I
(58)	53	F	+I
(59)	61	F	+I
(60)	61	F	+I
(61)	49	F	+I
(62)	70	M	+
(63)	33	M	+
(64)	63	M	+
(65)	51	M	+
(66)	73	M	
(67)	50	F	+
(68)	51	M	+
(69)	33	F	+

Erythrocytes	Leukocytes	Polymorphonuclears	Small Lymphocytes	Large Lymphocytes	Mast Cell	Wassermann	Eye-grounds	Basal Metabolism	Complications and Associated Diseases
		59	36	5		N			O
Mil	9.1 m.	70	20	10		N			O
		58	34	8		N			O
		70	26	4		N			Aneurysm Aorta (X-ray)
		63	25	12		N			O
		74	22	4		N			O
Mil	10.6 m.	78	16	5		N			Carcinoma-Gall-bladder?
		52	44	4		N			O
						N			O
		65	20	6		N			O
		70	24	6		N			O
		67	14	18	1	N			O
		70	20	9	1	N			O
		58	36	4	2	N			O
		60	24	16		N			Achlorhydria
		82	15	3		++++			General Paresis
		78	12	10		N			O
		60	28	11	1	N			O
		68	22	9	1	N			O
		56	33	10	1	N			Fistula in ano—Focal infection Tonsils
		62	29	9		N			O
		55	33	9	1	N			Blood Sugar 183%—Boils
		85	12		3	N			O
						N			Diabetes Mellitus
		72	26	2		N			O
						N			O
	10.4 m	76	20	4		N			Hyperchlorhydria
	6 m.	67	29	3	1	N			Cholecystitis Strep. Lyon-Meltser
		72	21	7		N			Enlarged Prostate. Pyelitis
		67	27	6		N			O
		80	15	5		N			Diabetes—B Sugar .192% Infected foot
		59	34	7		N			Blood Sug .09%
		62	25	6		N			Dilatation Arch. Aorta-X-ray
						N			O
		64	30	6		N			O
		80	11	9		N			Pulmonary Tuberculosis

ological product of metabolism which also causes marked involvement of the vessels in the arteriosclerotic process.

There are several facts which are opposed to the latter view: (1) Not infrequently the small and smallest blood-vessels of the kidney show arteriosclerotic changes in benign hypertension; (2) the inflammatory process occurs at all stages of the arteriosclerotic process—in the early as well as late cases; (3) occasionally a previous stage of benign hypertension is observed; (4) both conditions attack patients of the same age; (5) there is great similarity of the symptoms in both.

For these reasons Volhard is inclined to accept the possibility that the cause may be found in some physiologic product of metabolism which acts on an arteriosclerotic basis. The age and sex distribution may be seen in the following table:

Volhard and Fahr's Cases			Author's Cases	
Age	Male	Female	Male	Female
30–40	6	..	..	..
41–50	8	3	3	1
51–60	13	2	5	1
61–70	2	1	7	3
71–76	1	..	1	1
	30	6	16	6

In Volhard and Fahr's cases, there was a history of lead poisoning in 4; use of tobacco in 5; alcohol in 2; and typical gout in 3.

Symptomatology.—The onset is gradual. Usually benign hypertension has existed for several years before the nephritis manifests itself clinically in the impaired kidney function. Albuminuric retinitis is sometimes an early sign. It may develop before the inflammatory changes can be detected.

The symptoms with reference to the cardiovascular system are the same as those in benign hypertension. They all, however, tend to be more severe. The relative myocardial insufficiency which tends to remain stationary in benign hypertension here soon passes over into complete decompensation. Attacks of angina pectoris are more frequent. The nocturnal attacks of asthma pass over into pronounced edema of the lungs, which is associated with anginoid complaints, a feeling of constriction in the chest, etc.

The arterial symptoms of benign hypertension are also encountered in the combination form. The gross cerebral accidents—cerebral hemorrhage—are probably less frequent, but symptoms due to hemorrhages or softening, such as transitory aphasia, temporary facial paresis or hemiparesis with short-continuing paralysis without loss of consciousness, fainting and dizzy attacks with following deafness, astereognosis, mental blindness, etc., occur more frequently. Cheyne-Stokes' breathing is very frequently observed.

Psychical symptoms are much more apt to occur and to be more severe in the combination form. These may partake of an irritating or depressing nature. They may so dominate the picture as to obscure the renal-arterial nature of the disease. The patient may be nervous, irritable, unruly or violent; or melancholic, whiney, and quick to cry. They are filled with fears of death and live between hope and fear. They are critical, dissatisfied with everything and resist the orders of the physicians and nurses. Mental weakness becomes noticeable and they degenerate mentally very rapidly. Inability to concentrate is often complained of, fatigue is marked, comprehension is slow and drowsiness comes on.

Usually these symptoms come on slowly, but confused conditions, wandering ideas and hallucinations may come on quickly. They may suddenly become violent and disorientated as to time and place. These conditions are sometimes mistaken for general paresis.

The patients suffer from headache of a migrainous type and severe occipital headaches, the former probably an eclamptic equivalent, and the latter due to increased intracerebral pressure. Eclamptic uremia may also occur, though true uremia with azotemia is more frequent, and the certain end if not produced by vascular accident, myocardial insufficiency or terminal infection.

Physical Findings.—*General Appearance.*—In contradistinction to benign hypertension the general appearance and strength suffers early. Emaciation is quite marked and there may be a cachectic appearance as in the end stage of chronic diffuse glomerulonephritis. This may be found in early cases before the inflammatory and degenerative changes in the kidney have progressed very far. The skin assumes a rather characteristic grayish yellow color. There is not infrequently slight exophthalmos giving the face a Basedowan expression, which is that of a sick person. The least effort exhausts the patient.

Blood-pressure.—The highest values are observed in the malignant form, and as a rule they are persistently high, but showing the tendency to transitory rises as in benign hypertension.

Blood-pressure	Volhard and Fahr's Cases	Authors' Cases
Below 170 mm. Hg.	1	4
170–180 mm. Hg.	2	4
180–199 mm. Hg.	5	2
200–219 mm. Hg.	6	3
220–239 mm. Hg.	9	4
240–259 mm. Hg.	9	1
260–280 mm. Hg.	4	1
	36	19

The Heart.—The largest hearts are also found in this form of nephropathy. Vòlhard and Fahr found the largest heart weighing 1000 grams (2.2 lbs.). The average weight of 10 cases was 732 grams, against 570 grams in benign sclerosis in the male sex.

The clinical manifestations of enlargement are manifest. The apex is displaced downward and outward, is heaving in character; the aortic second is accentuated as are the sounds at the other ostia. Both presystolic and diastolic gallop rhythm may be encountered. All of the signs which are found in benign hypertension are also found here. There is possibly a greater tendency to arrhythmia. Cardiac edema is often present, but renal edema as in the benign form is absent.

LABORATORY FINDINGS.—*Urine.*—The urine presents quite a variable picture, depending largely upon the stage to which the superimposed nephritis has developed. In the early stage the color and quantity of the urine may be normal, except an abnormal variation between the day and night urine. With myocardial insufficiency the quantity decreases and the color and concentration increases. With the preservation of the heart strength and the progress of the nephritis the quantity increases both day and night with a fixed specific gravity, just as in the end stage of chronic diffuse glomerulonephritis. Often these changes in the urine may be followed while the case is under observation.

Albuminuria.—In the early cases it may be absent, but it soon appears and tends to be present in somewhat greater quantity than in benign hypertension. It may increase markedly as the result of chronic passive congestion of the kidney. It was absent in 3 of the author's cases, + in 15, + + in 1, and + + + in 1. *Sediment:* Casts are almost regularly found; they may be of all varieties. Leukocytes are regularly present, also epithelium, occasionally lipoids, and more rarely red blood-cells. *Blood:* In contrast to benign hypertension the blood constantly shows a secondary anemia which varies greatly in degree.

SPECIAL EXAMINATION.—*Ophthalmoscopic.*—Changes in the eye-grounds are the rule. As stated above, it may sometimes occur before there is evidence from the urine and other sources that nephritis is in progress. Neuroretinitis albuminurica is, of course, the change here referred to, but the arteriosclerotic changes described under benign hypertension may occur here.

Functional Kidney Tests.—These vary greatly, but they are usually impaired, this forming one of the pathognomonic signs of the malignant form. One of the earliest signs of kidney insufficiency is a night polyuria with a low specific gravity. With the progress of the disease, the modified Mosenthal test shows a day polyuria, fixed specific gravity, and low concentration of the salt and nitrogen of both the day and night urine. The phenolsulphonephthalein output is low, varying from the lower limits of normal to 0, in 2 hours and 10 minutes. In 7 of the author's cases in which it was estimated, the values were 26, 6, 3, 39, 8, 3, 5, and 0 per cent.

There is regularly nitrogen retention. The blood urea in 19 cases was 55.2, 52.5, 99.4, 58.5, 55.5, 53, 75, 61.5, 75, 67.5, 64.5, 122.5, 80, 88.6, 96.45, 153.75, 124.9, 68.2, and 321 mg. per 100 c.c of blood.

The same factors which affect the variation of the kidney function in chronic diffuse glomerulonephritis in the end stage also operate here. What was said there with respect to acidosis and the basal metabolic rate also obtains here.

Diagnostic Features.—(1) Occurs most frequently from 40 to 50 years of age and in men.

(2) The good general condition of benign hypertension rapidly declines and soon presents the characteristic cachectic condition of chronic nephritis.

(3) The disease runs its course as a cardiovascular renal disease. The cardiovascular symptoms as compared with benign hypertension and characterized by a tendency to greater severity.

(4) The blood-pressure is high and constantly maintained, showing the highest values.

(5) Cardiac hypertrophy is marked, comes on early and here we find the largest hearts.

(6) Edema when present is of cardiac origin.

(7) The blood shows marked secondary anemia in contrast to benign hypertension.

(8) The urine shows nycturia, a day and night polyuria, a low specific gravity, albumin, and cylindruria of moderate grades.

(9) Papillitis and neuroretinitis are the rule and are certain indications that the case does not belong to the type of benign hypertension, although the kidney functional tests may show little or no impairment.

(10) Impairment of kidney function is the chief characteristic of this type. This varies from the slightest to the most severe.

(11) If death does not occur earlier from the cardiovascular component of the disease or from a terminal infection, the end results from true uremia as in the end stage of chronic diffuse glomerulonephritis. Eclamptic equivalents are prominent as in benign hypertension, the psychical symptoms tending to be more severe. Eclamptic uremia rarely occurs.

Treatment.—Little more need be said of the treatment of the combination form than has been fully discussed in the treatment of benign hypertension and the various stages of kidney insufficiency in the section on the end stage of chronic diffuse glomerulonephritis (*q.v.*).

Prognosis.—The gradual nephritis of unknown etiology which attacks a previously arteriosclerotic kidney is in spite of timely treatment always an incurable disease and of unfavorable prognosis. If death does not occur earlier from myocardial insufficiency, a vascular accident or terminal infection, uremia is the certain outcome. A few months may decide this. After the nephritic component becomes decidedly manifest, the course rarely extends over more than a year or two.

Pathology.—MACROSCOPICAL.—The kidneys, as in benign hypertension, may be contracted or noncontracted, though in malignant hypertension the former is more frequent.

Of 23 cases coming to autopsy, Volhard and Fahr found the kidneys noncontracted in 7 cases, and contracted in 16 cases. In contrast to the noncontracted kidney of benign hypertension, the cortical markings are completely obscured; the limit between cortex and medulla is indistinct. The cortex is beset with numerous yellowish, smutty flecks and streaks. The outer surface often shows only a suggestion of flat granulation and is flecked with yellow brownish spots. The consistency is tough throughout, and on section the vessels stand open. In the contracted form, the outer surface shows regular, tolerably fine granulations which are grayish yellow in color. The interlying parenchyma is of a brown color. These conform to the red granular kidney of Jores; except in the pure arteriosclerotic form the cortical markings are recognizable.

MICROSCOPICAL.—The glomeruli in the atrophic areas undergo degeneration, as in the arteriosclerotic form, but these are more numerous and show much richer round cell infiltration. In the glomeruli there are also degenerative changes and occasionally a true inflammatory process.

The epithelium also shows fatty changes; fat droplets occur which run together to form large drops. Some of the fat crystals are singly refracting; but some doubly refracting crystals may be found. Also changes may be seen in the glomeruli which resemble the hyalin droplet degeneration of the tubular epithelium. Besides these degenerative changes other glomeruli show inflammatory changes; there may be small collections of leukocytes and in places the layers of the capsule may be adherent, while still other loops may contain fibrin and occasional red blood-cells.

Sometimes the inflammatory changes in the intracapsular space may assume the half-moon shape. Occasionally one sees the vasa afferentia, leading to the inflamed glomerulus, markedly changed by arteriosclerosis. The inflammatory changes in the glomeruli vary very much in intensity from case to case. The greater number of glomeruli in a section is free from inflammatory changes.

Fatty changes in variable intensity may be seen in the parenchyma; not rarely there are considerable accumulations of fat and double refracting substances in the interstitium, as well as dropsical degeneration in the epithelium of the convoluted tubules.

The changes in the vascular system are analogous to those described for arteriosclerosis except the small and smallest blood-vessels are more intensive and extensive.

The heart is markedly hypertrophied, as stated above, showing the weights greater than in any other nephropathy. Sclerosis of the coronary arteria is frequently found. This occurred in 14 of 23 cases of Volhard and Fahr. Other areas may be involved in the arteriosclerotic process, as in benign hypertension.

ILLUSTRATIVE CASE No. I.—J. E. H., male, white, age 50, married, chemist. Seen first at his residence, July 5, 1921.

Chief Complaint.—Severe pain in the abdomen.

Family History.—Father died of angina pectoris; mother is alive and has pernicious anemia; 5 sibs, 4 alive and well; 1 died of diphtheria.

Past History.—In childhood had measles, scarlet fever, much tonsillitis, tonsillectomy. Post childhood, as a young man had a great deal of malaria, nervous prostration 17 years ago. For the past 15 years, while he has not been confined to bed, has had a good deal of indisposition. He states that his urine has been examined at intervals of six months for several years and it has always been reported negative as to albumin.

Present Illness.—Last summer he began to go down. He seemed anemic and inert and displayed a lack of interest in things in general. Last spring, he had an attack of shortness of breath accompanied by wheezing in the chest. He has had pain in his abdomen more or less for 10 or 15 years. He thinks he has passed more urine than normal for several years. About two weeks prior to this date he had severe pain in the abdomen. This has gradually grown worse. It was for this symptom that he consulted a physician. Other symptoms with the exception of constipation are not noted.

Physical Examination.—The patient is an undernourished man, of pale appearance, and looks more than 50 years of age. Temperature 98° F. (36.66° C.), pulse 100 per minute, blood-pressure 220–160. Heart is hypertrophied. The eyes react to light and accommodation. The teeth are bad. The throat is red; the patient complains of soreness where the tonsils were removed several years ago. The neck is negative. *Abdomen:* There is pain on pressure in the region of the umbilicus; neither the liver nor spleen is palpable; the skin, bones and joints are negative, except for the pallor noted above.

Laboratory Findings.—*Urine:* Voided specimen, amber, clear, albumin, +; sugar, negative; casts, hyalin and finely granular + + +; red blood-cells +; pus cells +. *Blood:* Hgb. 72 per cent. (Sahli); red cells 4,330,000; white cells 12,400; polymorphonuclears 76 per cent.; small lymphocytes 14 per cent.; large mononuclears 8 per cent.; transitional 2 per cent. Wassermann negative.

Special Examinations.—X-ray showed stomach filled well, and somewhat hypertonic in type. Fairly good duodenal cap was obtained under fluoroscope. It emptied in about 5 hours. Small intestines showed spastic and dilated areas scattered along the entire tract. The appendix was very much dilated and did not fill well. The cecum and ascending colon retained barium for 3 days without any passing the hepatic flexure. Barium enema filled the entire colon, and this area showed no obstruction, but a very large colon with very little activity. Barium was adhering all along the course of the intestinal tract, indicating low grade colitis. The teeth showed marked pyorrhea with a small abscess of upper right central. The pain in the abdomen subsided under large doses of benzyl benzoate. He had no fever at any time.

MOSENTHAL (JULY 17, 1921)

Time	Quantity	Specific Gravity
10 A. M.	120 c.c.	1917
12 M.	240 c.c.	1015
4 P. M.	80 c.c.	1012
8 P. M.	180 c.c.	1015
Total day	620 c.c.	....
Total night	760 c.c.	1013
Total 24 hrs.	1340 c.c.	....
Total fluid intake	2500 c.c.	....

July 19, 1921, blood urea, 40.5 mg. per 100 c.c. Patient had been on a very low protein diet for several weeks. July 26, 1921, blood hemoglobin 65 per cent.; red cells, 3,300,000; white cells 17,600; polymorphonuclears 82 per cent.; small lymphocyte 11 per cent.; large mononuclears 7 per cent. Blood urea, 63.5 mg. per 100 c.c. *Urine:* August 16, 1920, clear, yellow, specific gravity 1012, acid, albumin and sugar negative, microscopically, hyalin casts, cylindroids, pus cells + +, epithelial cells +, red blood-cells + +. Blood urea 122.5 mg. per 100 c.c. The eye-grounds showed albuminuric retinitis. Signs of complete cardiac decompensation developed in the last 10 days or two weeks of his illness. The patient died of uremia.

Clinical Diagnosis.—Malignant hypertension, combination form (nephrosclerosis), angina abdominalis, myocardial insufficiency, and uremia.

ILLUSTRATIVE CASE No. II.—Mr. J. V. R., male, age 62, married, lumber business, March 4, 1921.

Chief Complaint.—Aching of legs on walking; fullness in chest on exercise. Duration 5 or 6 years.

Family History.—Father died of paralysis; mother, at 60, of kidney trouble; 5 sibs; one died of angina pectoris; one of paralysis.

Past History.—Had the ordinary diseases of childhood, a slight attack of dilatation of the heart 5 years ago. Has had erysipelas twice in the last two years.

Present Illness.—Feels pains in his legs on exercise and some fullness in the chest on exercise, no pain, no palpitation, no swelling of the feet. He has a slight cough, a good appetite, no indigestion, no colic and the bowels move regularly. No symptoms referable to the urinary system.

Physical Examination.—The patient is fairly well nourished. Temperature 98° F. (36.66° C.); pulse 78 per minute; blood-pressure 170–100. The head and neck are negative. The heart is hypertrophied. Apex in the sixth interspace, outside the midclavicular line. All of the palpable arteries are sclerotic. The abdomen and nervous system are without abnormal findings.

MOSENTHAL TEST

Time	Quantity	Specific Gravity
10 A. M.	172 c.c.	1012
12 M.	190 c.c.	1010
2 P. M.	130 c.c.	1010
4 P. M.	100 c.c.	1012
6 P. M.	190 c.c.	1010
8 P. M.	190 c.c.	1010
Total day	962 c.c.	....
Night urine	970 c.c.	1012
Total 24 hrs.	1932 c.c.	....
Total fluid intake	2000 c.c.	....

Albumin a trace, hyalin and granular casts. Phenolsulphonephthalein output, 20 per cent. in the 2 hours and 10 minutes. Blood urea, 80 mg. per 100 c.c. About six months after this examination the patient died suddenly from an attack of angina pectoris.

Clinical Diagnosis.—Malignant hypertension, combination form (nephrosclerosis), and angina pectoris.

ILLUSTRATIVE CASE NO. III.—Mr. C. L. C., male, 61, married, planter. Consulted author at his office, May 17, 1921.

Chief Complaint.—General weakness, tires very easily. Burning of feet, some dizziness, headache. Patient complains chiefly of high blood-pressure.

Family History.—Father died of blackwater fever; mother is dead, cause unknown. One brother died from high blood-pressure with paralysis; 4 sisters died of blackwater fever. One brother died of liver trouble and one of pneumonia.

Past History.—Has had measles, pertussis, typhoid fever, blackwater fever. His general health has been good until seven years ago. About four years ago he had some ear trouble—indefinite.

Present Illness.—For about seven years the patient has had attacks of dizziness; he walks with difficulty, especially in the dark. He has been gradually getting weaker—tires very easily. He has lost some weight, but does not know how much. He has marked shortness of breath and palpitation of the heart on exercise. He has not noticed any swelling of the feet or legs. He occasionally has pain below the right costal border, gets a little yellow and has "bilious attacks" at times. The pains have no reference to eating. He is very constipated. He thinks his urine is scant and he has to get up several times at night to void. He has a cramping sensation in the right arm and hand and some ringing in the ears.

Physical Examination.—The patient is very much undernourished and presents a pale appearance. Temperature 98° F. (36.66° C.); pulse is 72 per minute and regular. Blood-pressure is 260–110. There is visible pulsation in the vessels of the neck. The aorta is palpable in the suprasternal notch and the supracardiac area of dulness is widened. The apex is in the seventh intercostal space, 1½ ins. (3.81 cm.) outside the midclavicular line. At the apex, there is a systolic thrill and murmur; the latter is heard in the back. There is a systolic thrill over the aortic area at the base and the aortic second is markedly accentuated. The lungs are negative. The liver is palpable below the costal margin, the spleen is not palpable. The pupils and reflexes are normal. *Urine (Voided Specimen):* Pale, yellow, acid, specific gravity 1010, albumin a trace, sugar negative, microscopically, casts +, epithelial cells +, a rare pus cell. *Blood (Stained Specimen):* Anisocytosis, polychromatophilia, polymorphonuclears 70 per cent., small lymphocytes 24 per cent., large mononuclears 6 per cent., Wassermann 3 +.

Kidney Function.—Phenolsulphonephthalein, 5 per cent. in 2 hours and 10 minutes. Blood urea, 85 mg. per 100 c.c.

Clinical Diagnosis.—Malignant hypertension, combination form (nephrosclerosis), and relative myocardial insufficiency.

ILLUSTRATIVE CASE NO. IV.—Mr. A. P. L., age 54, married, merchant-farmer. Consulted author at his office, August 17, 1921.

Chief Complaint.—Partial paralysis right side of body, following stroke two years ago. Indistinctness of speech. Shortness of breath and palpitation.

Family History.—Father died of Bright's disease; mother died of childbirth; one sib died of pneumonia, one of heart disease, one of pneumonia, and one of typhoid fever.

Past History.—Measles, mumps, pertussis, typhoid fever, has had a few attacks of bilious colic accompanied by jaundice, and a stroke of paralysis two years ago.

Present Illness.—About two years ago he had an attack of paralysis of the right side of the body. This came on gradually without loss of consciousness. This is much better now, but he still has some difficulty in using the right arm and leg and his speech is indistinct. He has marked shortness of breath and palpitation on exercise, but no swelling of his feet. He has nausea and a heavy feeling in the epigastrium two or three hours after eating. He rarely vomits, is constipated, and his appetite is poor. He has been losing weight rapidly lately, about 40 pounds in the last few months. Symptoms referable to the urinary system are negative.

Physical Examination.—The patient is fairly well nourished, though losing weight. Temperature 98.4° F. (36.77° C.); pulse 108; blood-pressure 240–150. The few teeth he has left are in fair condition. The left tonsil is very ragged and infected. Marked atrophy of the muscles of the right chest. *Heart:* The apex beat is heaving in the sixth intercostal space, one inch (2.54 cm.) outside the midclavicular line; the heart sounds are clear and there is marked accentuation of the aortic second. The palpable vessels are sclerotic. The abdomen is negative. The pupils are equal and react to light; the mouth is drawn somewhat to the left; the tongue deviates a little to the left on protrusion. Some impairment of strength in grip of right hand. Knee-jerks are exaggerated on both sides, but markedly so on the right as are also arm jerks. Babinski slightly positive on both sides. Eye-grounds—arteriosclerosis, hemorrhage and albuminuric retinitis.

Laboratory Findings.—Urine (voided specimen), cloudy, yellow, specific gravity 1012, acid, albumin +, sugar negative, microscopically, red blood-cells + +, epithelial cells +, motile bacilli +, casts + +. Blood (stained specimen): anisocytosis; differential count, polymorphonuclears 79 per cent., small lymphocytes 15 per cent., large mononuclears 6 per cent. Wassermann, negative.

Functional Tests.—Phenolsulphonephthalein, 6 per cent. in 2 hours and 10 minutes. Blood urea, 61.5 mg. per 100 c.c.

Clinical Diagnosis.—Malignant hypertension, combination form (nephrosclerosis), old hemiplegia, and relative myocardial insufficiency.

BIBLIOGRAPHY

Congenital Nephropathies

ANDERS, J. M. Congenital single kidney, with the report of a case; the practical significance of the condition, with statistics. Jour. Amer. Med. Sc., March, 1910, cxxxix, 1.

BRAASCH, W. F. The clinical significance of congenital anomaly in kidney and ureter. Ann. Surg., 1912, lvi, 726.

COPLIN, W. M. L. Unilateral renal hypoplasia and dysplasia due to defective arteriogenesis; relation to so-called hypogenetic nephritis. Jour. Amer. Med. Sc., March, 1917, cliii, No. 3, p. 381.

EISENDRATH, D. N. Clinical importance of congenital anomalies of the kidney. Surgical Clinics, Chicago, October, 1917, l, 1053.

GERAGHTY, J. F., and PLAGGMEYER, H. G. The practical importance of infantile kidneys in renal diagnosis. Jour. Amer. Med. Assoc., 1913, lxi, 2224-2228.

GIBBON, J. W. Anomalies of the kidney and ureters and their embryological significance. Jeffersonian, Phila., 1916, xvii, 1-9.

KEIBEL AND MALL. Human embryology. Vol. II. J. B. Lippincott Co., Philadelphia and London, 1912.

KELLY AND BURNAM. Diseases of the kidneys, ureters, and bladder. Vol. II. D. Appleton & Co., New York City, 1914.

MAYO, C. H. The surgery of the single and horseshoe kidney. Ann. Surg., April, 1913, lvii, pp. 511-521, 6 pl.

NEWMAN, D. Malformations of the kidney and its displacements without mobility with illustration of cases and specimens. Transactions Clinical Society, London, 1897-1898, xxxi, 118-157.

——— Horseshoe kidney. Lancet, London, 1917, ii, 236.

——— Pain in renal and vesical lesions. Lancet, London, 1916, i, 669-724.

ROLLESTON, J. D. Single pelvic kidney. Brit. Jour. Child. Dis., London, 1916, xiii, 80-86.

STEIN, A. The clinical importance of unilateral fused kidney (including the dystopic kidney of one side). Amer. Jour. Obstet. and Dis. Wom. and Child., March, 1916, lxxiii, 449.

Blood										
Red Cells	Leukocytes	Polymorpho-nuclears	Small Lymphocytes	Large Mononuclears	Eosinophils	Mast Cell	Wassermann	Eye-grounds	Basal Metabolism	Complications and Associated Diseases
		67	29	4			N	N		O
		76	21	3			N			O
3.8 Mil.	5.8 m.	71	23	6			N			O
							N			Been on diet for a year for alb.—sug. Diabetes
		71	16	9	3	1	N			?
		66	25	7		2	N			Beginning
		57	37	6			+++			Syphilis
3.75 Mil.	6 m.	71	28	1			N			O
		79	15	6			N			
		70	24	6			+++			Syphilis
		52	42	6			N			O
		81	15	4			N			Widened Aorta
4.1 Mil.		72	19	9			N			O
4.3 Mil July 5 3.3 Mil July 19		76 82	14 11	10 7			N			O
							N			O
							++++			Syphilis
										O
										O
							++++			Syphilis
										O

indicates *not present.*

Movable Kidney

Behan, R. J. Pain. D. Appleton & Co., New York, 1914.

Bryan, R. C. A few further remarks on the pathology and diagnosis of a dislocated or movable kidney. International Clinics, iii, 27th Series, p. 116.

Harris, M. L. Movable kidney. Transactions of American Surgical Association, 1901, xix, 457.

Kelly and Burnam. Diseases of kidney, ureter and bladder. Vol. I. D. Appleton & Co., New York City, 1914.

McAlister, A. Nephroptosis. In Allbutt and Rolleston's System of Medicine, Vol. IV, Pt. I. The Macmillan Company, London, 1908.

Newman, D. Pain in renal and vesical diseases. Lancet, London, 1916, i, 773.

Piersol, G. A. Human anatomy. Vol. II. J. B. Lippincott Co., Phila., 1918.

Barker, L. F. Monographic Medicine. Vol. III. D. Appleton & Co., New York City, 1916.

Uremia

Ascoli, G. Vorlesungen über Uraemie. G. Fischer, Jena, 1903.

Bradford, J. R. General pathology of renal disease. System of Medicine, Allbutt and Rolleston. Vol. IV, Part I. The Macmillan Company, London, 1908.

Chace, A. F. Diet in interstitial nephritis. Med. Clinics N. America, Nov., 1917, i, 611.

Foster, N. B. Uremia. III. The non-protein nitrogen of the blood. Arch. Int. Med., Chicago, 1915, xv, 356-368.

Foster, N. B., and Davis, H. B. The effect of water intake on nitrogen retention in nephritis. Amer. Jour. Med. Sc., Phila., 1916, cli, 49-63.

Herringham, W. P. Treatment of uremia: kidney diseases. Oxford Medical Publications, London, 1912.

Howland, J., and Marriott, W. McK. Observations on acid-base equilibrium in the body. Amer. Jour. Physiol., Boston, 1916-1917, xlii, 587.

Osler, Sir Wm. Transient attacks of aphasia and paralysis in states of high blood-pressure and arteriosclerosis. Canadian Med. Assoc. Jour., 1911, i, 919.

Pal, J. Gefässkrisen. S. Hirzel, Leipzig, 1905.

Vaquez, H. La tension arterielle dans le saturnisme aigu et chronique. Semaine méd., Par., 1904, xxiv, 385.

Volhard, F., and Fahr, T. H. Die Brightsche Nierenkrankheit. Julius Springer, Berlin, 1914.

Circulatory Nephropathies

Allbutt, Sir C. Diseases of the arteries, including angina pectoris. Vol. I. The Macmillan Company, London, 1915.

Barker, L. F. Circulatory insufficiency. Monographic Medicine. Vol. II. D. Appleton & Co., New York, 1916.

Gibson, A. G. Insufficiency and dilatation of the heart. Modern Medicine, Osler and McCrae. Vol. IV. Lea and Febiger, Philadelphia and New York, 1915.

Hewlett, A. W. Functional pathology of internal diseases. Monographic Medicine. Vol. I. D. Appleton & Co., New York and London, 1916.

Hürter. Untersuchungen am arteriellen menlischen Blute. Deutsch. Arch. f. Klin. Med., 1912, cviii, 1.

Lewis, T., Ryffel, J. H., Wolf, C. G. L., Cotton, T., and Barcroft, J. Observations relating to dyspnea in cardiac and renal patients. Heart, 1913, v, 45.

McCallum, W. G. Cardiac valvular disease and its consequences in a textbook of pathology. W. B. Saunders Company, Philadelphia, 1916.

McKenzie, Sir J. Chronic diseases of the heart. Oxford Medicine. Vol. II. Oxford University Press, London, 1920.

Mosenthal, H. O. Renal functions as measured by the elimination of fluids, salt and nitrogen, and the specific gravity of the urine. Arch. Int. Med., Chicago, 1915, xvi, 733-774.

Rowntree, L. G. The treatment of nephritis. Practical Treatment. Vol. IV (The newest treatment). W. B. Saunders Company, Philadelphia, 1917.

Siebeck, R. Die funktionelle Bedeutung der Atemmechanik und die Lungenventilation bei Kardialer Dyspnoe. Deutsch. Arch. f. Klin. Med., 1912, cvii, 252.

The Nephropathies Generally Included Under the Genetic Term Bright's Disease

Adami, J. G. Inflammation. The Principles of Pathology. Vol. I (General pathology). Lea and Febiger, Philadelphia and New York, 1908.

Allbutt, Sir C. Loc. cit. supra.

Aschoff, L. Harnapparat. Pathologische Anatomie, Dritte Auflage, Bd. II, Gustav Fischer, Jena, 1913.

Councilman, W. T. Acute interstitial nephritis. Jour. Exp. Med., N. Y., 1898, iii, 305-420.

Fahr, T. H. Über chronische Nephritis und ihre Beziehung zur Arteriosklerose. Virch. Arch., 1909, Bd. 195, 228.

Gaskell, J. F. On the changes in glomeruli and arteries in inflammatory and arteriosclerotic kidney disease. Jour. Path. and Bacter., Cambridge, July, 1911, xvi, 287-321.

Janeway, T. C. A clinical study of hypertensive cardiovascular disease. Arch. Int. Med., 1913, xii, 755.

Jores, L. Über die Arteriosclerose der kleinen Organarterien und ihre Beziehung zur Nephritis. Virch. Arch., 1904, Bd. 178.

Lohlein, M. Über die entzündlschen Veränderungen der Glomeruli bei menschlichen Nieren und ihre Bedeutung für die Nephritis. S. Hirzel, Leipzig, 1906.

——— Über hämorrhische Nierenaffectionen bei chronischer ulceröser Endocarditis (Embolische, nicht Eitrige Herdnephritis). Med. Klin., 1910, Nr. 10.

Lubarsch. Entzündung. In Aschoff's Allgemime pathologische Anatomie. Vol. II, 374, cit. supra.

Müller, F. Morbus Brightii. Deutsch. patholog. Gesellsch., *Meran,* 1905.

Reichel, H. Über Nephritis bei Scharlach. Zeitschr. f. Heilk., 1905, xxvi, Heft I, 72.

Ribbert, H. Über Nephritis und über Entzündung parenchymatoser Organe. Deutsche. Med. Wchnschr., 1909, Nr. 46, p. 1996.

Volhard and Fahr. Loc. cit. supra.

Weigert, C. Gesammelte Abhandl., Berlin.

Nephroses

Epstein, A. A. Edema in chronic nephritis. Amer. Jour. Med. Sc., Nov., 1917, cliv, 638.

Foster, N. B. Loc. cit. supra.

Fischer, M. H. Edema. Wiley and Sons, New York, 1910.

Heineke, A. Veranderungen der menschlichen Niere nach Sublimalvergiftung. Ziegl. Beitrag., Bd. 45.

Hewlett, A. W. Loc. cit. supra.

McCallum, W. G. Loc. cit. supra.

Ophüls, W. Nephritis; a new series of cases with a review of recent literature. Jour. Amer. Med. Assoc., Chicago, 1915, lxv, 1719-1725.

Munk, F. Klinische Diagnostik der degenerativen Neirenkrankungen. Zeitschr. f. Klin. Med., Berl., 1913, lxxviii, 1, 1 pl.

Newburg, L. H. Production of Bright's disease by feeding high protein diet. Arch. Int. Med., October, 1919, xxiv, 359.

Pearce, R. M. The production of edema; an experimental study of the relative etiology, etc. Arch. Int. Med., Chicago, 1909, iii, 422-437.

Volhard und Fahr. Loc. cit. supra.

The Glomerulonephritides

Baehr, G. Significance of embolic glomerular lesions of subacute streptococcus endocarditis. Arch. Int. Med., Feb., 1921, xxvii, 262.

Eppinger, H., and **Kloss**, K. Die Nephritisfrage. Velag von Moritz Perles, Wein, 1921.

Herrick, J. B. Nephritis. Modern Medicine. Osler & McCrae, 2nd Edition, Vol. III. Lea & Febiger, Philadelphia and New York, 1914.

Janeway, T. C. Nephritic hypertension; clinical and experimental studies. Amer. Jour. Med. Sc., Phil. and New York, 1913, cxlv, 625, 656.

——— Management of patients with chronic renal disease. Bull. Med. and Chir. Fac. Univ. Maryland, Baltimore, 1916, viii, 103-122.

Hulse, W. Volhard's theory of glomerulonephritis. Deutsche med. Wchnschr., Nov. 4, 1920, xlvi, 1244.

Hewlett, A. W. Loc. cit. supra.

Lohlein, M. Über Nephritis nach dem heutigen Stande der pathologisch-anatomischen Forschung. Ergebn. d. inn. Med. und Kinderh., Berlin, 1910, v, 411-458.

Müller, F. Loc. cit. supra.

Orth, A. Pathologische Anatomie, Bd. II.

Ophüls, W. Loc. cit. supra.

O'Hare, J. P. A nephritic diet sheet. Amer. Jour. Med. Sc., 1920, clix, 883.

Siegl, W. Experimentelles zur Frage der Erkältungsnephritis. Verh. d. xxv Kongr. f. inn. Med., 1908.

Von Noorden, C. Clinical treatises on the pathology and therapy of disorders of metabolism and nutrition. Part II. Nephritis. E. B. Treat and Co., New York, 1903.

Christian, H. S. Nephritis. In Oxford Medicine. Vol. III. Oxford University Press, London and New York, 1920.

Volhard and Fahr. Loc. cit. supra.

Scleroses

Barker, L. F. The causes and treatment of the conditions underlying high blood-pressure. Ohio State Med. Jour., October, 1920, xvi, 709.

Jores, L. The commoner diseases, their causes and effects. Woglom-Lippincott, 1915.

Meara, F. S. Hyperpiesia of Clifford Allbutt (essential hypertension). Med. Clinics North America, No. 1, W. B. Saunders Co., Phila. and London, 1918-1919, ii, 1.

Volhard und Fahr. Loc. cit. supra.

Allbutt, Sir T. C. Loc. cit. supra.

Janeway, T. C. Loc. cit. supra.

CHAPTER II

DISEASES OF THE KIDNEY

BY ANTON G. RYTINA, A.B., M.D., F.A.C.S.

Pyelitis, p. 691:—Definiton, p. 691; Classification, p. 692; Etiology, p. 692; Symptoms and course, p. 694; Diagnosis, p. 695; Treatment, p. 696; Pathology, p. 699.
Pyonephrosis, p. 700:—Definition, p. 700; Etiology, p. 700; Symptomatology, p. 701; Diagnosis, p. 702; Treatment, p. 702; Prognosis, p. 703; Pathology, p. 703.
Perinephritic abscess, p. 704:—Definition, p. 704; Etiology, p. 704; Symptomatology, p. 705; Diagnosis, p. 705; Treatment, p. 706; Prognosis, p. 706; Pathology, p. 706.
Hydronephrosis, p. 707:—Definition, p. 707; Etiology, p. 707; Symptomatology, p. 708; Diagnosis, p. 709; Treatment, p. 710; Prognosis, p. 711; Pathology, p. 711.
Kidney and ureteral stone, p. 712:—Definition, p. 712; Etiology, p. 712; Symptomatology, p. 715; Diagnosis, p. 716; Treatment, p. 718.
Calculous anuria, p. 720:—Definition and onset, p. 720; Symptomatology, p. 720; Diagnosis, p. 721; Treatment, p. 721; Pathology, p. 722.
Cysts of the kidney, p. 722:—Classification, p. 722:—Multiple small cysts, p. 722; Large serous cysts, p. 722; Polycystic degeneration, p. 723; Dermoid cysts, p. 725; Paranephritic cysts, p. 725; Echinococcus cysts, p. 725; Tubercular cysts, p. 724.
Renal tumors, p. 727:—Introductory, p. 727; Benign renal tumors, p. 727; Malignant renal tumors, p. 729; Bibliography, p. 735.

PYELITIS

(Pyelonephritis)

Definition.—Pyelitis is an inflammation of the kidney pelvis due to microbial infection. When one considers the frequency with which the term pyelitis is used, one would hardly realize that cases of pure pyelitis never occur, because bacteriological and pathological studies have shown the impossibility of having a pyelitis without an associated nephritis, so that the proper term should not be pyelitis, but pyelonephritis. However, from a clinical standpoint, there are certain cases in which inflammation of the pelvis is the dominating factor rather than the infection in the kidney, which may be trivial. Cases of this type respond better to treatment and are often curable, whereas cases of pyelonephritis do not offer the same chances for radical cure under treatment to be outlined later. The term dates from the time of Rayer, and has become so fixed as the word to describe the clinical condition of the mild or nonsurgical forms of pyelonephritis that it does not seem wise to discontinue it. Strictly speaking, every grade of kidney infection represents different degrees of the same process.

Classification.—Kretschmer divides pyelitis into the following clinical groups: (1) Defloration pyelitis, or the type occurring in newly-married women; (2) pyelitis of infancy and childhood; (3) pyelitis of pregnancy; (4) pyelitis following surgical operations; and (5) cases of simple pyelitis. Symptomatically, it is divided into the acute, subacute, and chronic forms.

Etiology.—Pyelitis is practically always caused by bacterial invasion and multiplication. Traumatism, elimination of certain irritant drugs, such as cantharids, cubebs, urotropin, etc., the alteration of the urine in certain diseases (sugar in diabetes) may cause renal congestion but not septic inflammation. Normally, the kidney can eliminate without harm to itself any variety of organism, the latter being carried to it by the blood current from a focus such as a purulent prostate or urethra, the bladder, intestine or from some far distant focus, *e. g.*, infected tonsils. In order to set up infection in the kidney or kidney pelvis, various factors are usually present, *e. g.*, a lowering of its resistance as a result of some general cause, such as anemia, overwork, worry, malnutrition or intercurrent disease. Pyelitis may be found in the course of various infectious diseases. Most commonly found, however, in the production of a pyelitis is obstruction in the urinary tract, which not only lowers the resistance of the kidney pelvis, but affords a favorable culture medium for the growth of various microörganisms. Obstruction alone though, in the urethra, bladder, or ureter will not cause suppurative pyelitis, but only a predisposition to it. For example, an aseptic ligation of one ureter leads to compression atrophy of the kidney on the corresponding side, whereas septic ligation is followed by suppurative processes. From what has been said, therefore, it is obvious, that certain factors are generally present before a pyelitis is set up, *viz,* lowered resistance, urinary obstruction and pyogenic microörganisms. The healthy mucous membrane of the urogenital tract ordinarily resists septic infection, but there are exceptions to this rule and at times pyelitis will be set up without any apparent or discoverable cause. The most frequent cause of pyelitis is infection by the bacillus coli communis. Next in importance are the staphylococcus aureus or albus, usually the former, and the streptococcus. Other organisms, such as bacillus of typhoid fever, bacillus proteus, gonococcus, pneumococcus, bacillus mucosis capsulatis, bacillus pyocyaneous, etc., are rather uncommon invaders. It is not uncommon to find one or more types of organisms associated in the condition, particularly in the advanced stages of the disease. Infections with the tubercle bacillus are quite common, but on account of the importance of the condition it is described separately.

Methods of Invasion.—The portals of entry are (1) hematogenous (descending); (2) urogenous (ascending); and (3) directly from without, as in wounds of the kidney. Regarding the first two methods of invasion, *viz.*, hematogenous and urogenous, there has been much discussion in the literature. For a long time, it was thought that in practically every case the infection was urogenous (ascending), the organisms traveling upwards from the lower genito-urinary tract either by way of the lumen of the ureter, or that they ascend from the bladder, prostate, etc., to the kidney pelvis through the lymphatics connecting these organs along the wall of the ureter (Eisendrath and Schultz). It is practically settled that ascending infection by way of the lumen of the ureter never occurs unless an almost complete obstruction exists, or unless we are dealing with the rare type of ureter mouth that permits regurgitation upwards of fluids from the bladder to the kidney pelvis. In a normal bladder, there is no reflux of urine from the bladder to the kidney. It was at one time thought that this was due to the oblique direction of the ureter in the bladder wall. However, it is easy to show that this same reflux does not occur following the operation of ureter transplantation. If ascending infection occurs, therefore, we must conclude that the paths along which the infection travels must be through the lymphatics of the wall of the ureter and of the renal pelvis. That this method of infection occurs is undoubted, but of recent years the importance of this method of invasion is considered greatly exaggerated and has given way to the hematogenous theory of invasion. According to this theory, in the vast majority of pyelitis cases, the infection is blood-borne. The chief advocates of this theory are Cabot and Crabtree. According to these authorities, colon bacilli circulate in the blood during the early hours of symptoms due to colon pyelonephritis and can be demonstrated by blood culture. In a limited number of these cases blood infection has been demonstrated to be primary, followed in order by albuminuria, bacilluria and pyuria. The portal of entry of bacillus into the blood stream is not always demonstrable. The intestine, a purulent urethra or prostate, or an inflamed bladder, are the commonest sources of bacilli. Even in cases where the infection may have taken place along the course of the lumen of the ureter, owing to an incompetent ureterovesical valve or from lymphatic extension, Cabot and Crabtree were able to recover the bacilli from the blood stream, causing them to seriously doubt the occurrence of renal infection without the intervention of the blood stream. A third but rare portal of entry in pyelitis is directly from without, as is wounds of the kidney.

PREDISPOSING CAUSES.—*Age.*—Pyelitis may occur at any period of life, although the largest number of cases that come under observation are seen in adults. Recent observations have shown that pyelitis in infants and children is rather common. Many cases of so-called cystitis in children are in reality cases of pyelitis, as it is rare to find pure cystitis in children without concomitant pyelitis. Pyelitis may occur at any age, from a short time after birth up to seventy-five years of age. The largest number of cases, however, occur between the ages of thirty-one and forty (25 per cent.). The next largest number of cases occur between the ages of twenty-one and thirty (about 20 per cent.). From this it will be seen that practically one-half of the cases occur between the ages of twenty and forty.

Sex.—At one time renal infections in women were supposed to be rare. In recent years, however, owing to the perfection of modern urological diagnostic methods the contrary has been proven. Indeed, if ones takes into consideration the number of cases of pyelitis which are seen in women, such as pyelitis occurring during and after pregnancy, pyelitis in female babies and children, the association of renal infection with lesions of the female generative organs, and the onset of renal infection after extensive gynecological operations, one may safely say that renal infections occur more frequently in women than in men. According to Kretschmer's studies, 61 per cent. of pyelitis occurs in females and 39 per cent. in males. Pyelitis is most often bilateral (about 60 per cent. of the cases). In the remaining 40 per cent. of the cases, the pyelitis is unilateral—the right kidney being more often involved than the left kidney.

Symptoms and Course.—The disease may be acute, subacute, or chronic. All are usually preceded by disease in the kidneys or other organs, even though at times they are not discoverable.

Acute Pyelitis.—Acute pyelitis usually begins with chills, high fever, and sweats. The temperature may reach as high as 105° F. (40.6° C.). The type of fever in acute pyelitis is not characteristic. It may be continuous, intermittent, or remittent. The height of the temperature does not depend upon the severity of the case and bears no special relation to the amount of pyuria and bacilluria. The constitutional phenomena usually attendant upon any febrile affection are present. The tongue is dry, thirst is experienced, and there is hebetude. Nausea and vomiting either alone or combined, severe pallor and marked prostration may develop. The urine contains much pus, many bacteria, heavy albumin ring, and some red blood-cells. Casts are not present in pyelitis, nor do they occur in pyelonephritis as a rule. Their constant presence points toward pyelonephritis, but their absence does not exclude the possibility of the latter affection. As a rule pain referable to the kidney is not found. Occasionally, however, the renal region is sensitive and rarely a distinct renal colic may be complained of. If renal sensibility becomes marked, persists, and if the chills and fever recur, suspicion concerning the formation of a kidney abscess is in order, and the same should be watched for. The urinary symptoms do not exhibit anything characteristic and may be present in any number of affections of the urinary tract. The urinary symptoms are mostly due to an attendant bladder involvement and consist in frequency, burning of urination, painful urination, urgency, difficulty and incontinence of urine. These symptoms may also be present, even though there is no cystitis present. Death occurs, sometimes within a short period, from coma, often with typical uremic convulsions. In other cases, the fever subsides suddenly as if by crisis, or it may become remittent in character; in still others it gradually reaches normal and the patient recovers or passes into the chronic stage.

Chronic Pyelitis.—It is not uncommon for the acute type to lapse into the chronic form. More frequently, however, the latter form develops insidiously without being preceded by the acute process. It should be remembered that chronic pyelitis may exist over a number of years without a history of fever or urinary disturbance and be diagnosed accidently on finding pus or bacteria in the urine. More commonly, however, the patients in addition to the physical findings in the urine have certain urinary symptoms referable to the bladder, *e. g.*, frequency, painful and burning urination, urgency, hesitancy, dribbling, or incontinence of urine. The latter symptoms frequently lead to the diagnosis of cystitis, and very often the patients have been subjected to local treatment referable to the bladder over a long period of years without benefit. It is a good rule to subject every patient suffering with urinary symptoms and changes to a ureter catheterization, unless the vesical origin of the affection is made practically certain by the finding of organic disease in or around the bladder, *e. g.*, prostatic hypertrophy, stricture, gonorrhea, and spinal cord disease. Even in these cases, a pyelitis may also be present. The physical findings of the urine are practically the same as described under acute pyelitis. The presence of red blood-cells may be absent. If the drainage of pus from the kidney is hampered by inspissated pus and the ureters partly or entirely obstructed, symptoms of acute pyelitis may be set up. Similarly, if the focus of infection is not located, exacerbation may occur and convert the chronic type of pyelitis into a temporary, acute form.

Diagnosis.—The diagnosis of pyelitis as a rule is not very difficult. Even before the diagnosis of pyelitis is made, it is necessary that the patient be subjected to a careful examination, not only of his urine, but the use of the cystoscope, ureter catheter, x-ray, functional test, wax tip bougie, and the pyelogram are necessary, in order to exclude the possibility of some organic lesion of the urinary tract being responsible for the pyelitis. Urine examination reveals urine that is cloudy, and shows a marked ring of albumin. Macroscopically the cloudiness is due to pus and bacteria. Usually a few red blood-cells and desquamated, epithelial cells are found in the urine. By means of the cystoscope and double ureter catheter examination, not only the condition of the bladder is ascertained, but the source of the pus, whether from the right side, left side, or both sides, is learned. Having determined this point, the next step is concerned with the differentiation of the various lesions which are associated with pyuria and pus in the urine. Lesions such as ureter stricture and stone, renal calculus, renal tuberculosis, tumor, hydronephrosis, must be eliminated. By means of the plain x-ray and the wax tip ureteral bougies, stone in the kidney and ureter must be eliminated. However, in rare instances, even the possibility of small stones in the kidney or ureter may be overlooked. Every case of pyelitis should be potentially considered as one of renal tuberculosis, masked by the presence of the colon bacillus. The elimination of a diagnosis of tuberculosis should be obtained not only by careful microscopic and bacteriological examinations of the urine, but repeated guinea pig inoculations should be carried out. The suspicion of kidney tuberculosis is increased by the presence of changes in the bladder, particularly near the ureteral orifice of the affected side, seen through the cystoscope. However, kidney tuberculosis, masked by colon bacillus in the urine with negative cystoscopic findings, may be obtained. Stricture of the ureter, large hydronephrosis, and renal tumor, could be differentiated by the pyelogram. Another important point in the diagnosis of pyelitis is the carrying out of separate or relative functional kidney tests. In pyelitis, the phenolsulphonephthalein output from each kidney is practically normal. both from the point of time of appearance and quantitative output, but in pyelonephritis, especially if it is quite marked and very far advanced, there is a decided **reduction** in the quantitative phenolsulphonephthalein output. Their differentiation has not only a decided value in differentiating pyelitis from pyelonephritis, clinically speaking, but has a definite prognostic significance in enabling us to predict whether or not treatment is going to prove curative. Because, in the cases of almost pure pyelitis, radical cure is often obtained, but only rarely so in the pyelonephritic types.

Treatment.—In cases of acute colon bacillus pyelitis, instrumental or local treatment is ordinarily contra-indicated. Treatment should consist of **rest**, and careful regimen of the **diet**, **forced water by mouth**, and **hexamethylenamin** by mouth in doses of from 7.5 to 10 grains (.4924 to .65 gram) every four hours. Proper attention should be given to the gastro-intestinal tract, and particularly the **avoidance of constipation** and the use of **free catharsis**. There may be exceptions to the rule of not using local or instrumental treatment in acute pyelitis. For example, the author has succeeded in relieving the streptococcus septicemia of pregnancy accompanied by high fever and marked prostration by pelvic lavage, with the result of not only relieving the patient of her severe symptoms, but allowing her to go to the termination of a normal pregnancy. The cases of pyelitis of pregnancy seem to have more marked constitutional symptoms than the ordinary cases. Very often acute pyelitis will not respond to this method of treatment, and the case will lapse into the chronic type.

The treatment of subacute or chronic cases of pyelitis may be considered under the following heads: (1) Medical treatment; (2) vaccine therapy; and (3) pelvic lavage.

MEDICAL TREATMENT.—The treatment of pyelitis by drugs has but a small place. Various drugs have been recommended, such as the administration of bicarbonate of soda, ½ to 1 teaspoonful, well diluted, three times a day. Salol has been highly recommended by some, but it has very little practical value. The only drug which is used by practically everyone is hexamethylenamin 7.5 to 10 grains (.4924 to .65 gram), well diluted in water every four hours. Its value is doubtful, as Hinman has shown that urotropin has little action at the level of the kidney pelvis. The acidity of the urine should be tested by examination with litmus paper, and if there is definite alkalinity, about 10 grains (.65 gram) of **acid sodium phosphate** should be given every four hours until the urine becomes acid, for the well-known reason that hexamethylenamin has no sure therapeutic value unless it acts in an acid medium. If for example, in some cases, urotropin causes vesical irritation or the production of hematuria and is contra-indicated, **benzoic acid** should be substituted. From a medical or internal standpoint, however, more important than the drug administration is the **drinking of large quantities of water.** Lithiated spring waters or other proprietary waters have no greater value than ordinary drinking water, unless it be given for its psychological effect.

VACCINE THERAPY.—Vaccine therapy has been given a thorough trial in the treatment of pyelitis, but has given the same futile results in this disease that it has given in most diseases wherein it has been tried. However, there are a number of authorities who believe in their efficacy and highly recommend them. A certain percentage of cases of pyelitis get well without any treatment whatever, and it is quite probable that cases of pyelitis which respond to vaccine therapy really belong to this class.

PELVIC LAVAGE.—Of all the various forms of treatment that have been used from time to time in the treatment of pyelitis, the latest form of treatment and one which has stood the test of time and which is undoubtedly the most effective, is that of **pelvic lavage.** This method of treatment consists in the **catheterization of the ureters** on one or both sides, depending upon whether the infection is unilateral or bilateral; then there is made a test of the capacity of the kidney pelvis by the introduction of sterile water through the syringe, followed by the introduction of a smaller amount of some medicated solution, usually from 8 to 10 c.c. injected through the catheter into the kidney pelvis. A large number of different drugs have been used for this purpose, for example, aluminum acetate, the organic silver salt preparations, such as colargol, argyrol, cargentos, silvol, etc. There is one drug, however, which has a more or less specific action on pyelitis when introduced into the kidney pelvis through the ureter catheter, namely, **silver nitrate.** The strength of the silver nitrate is from 1 to 2 per cent.; in most instances a 1 per cent. solution will suffice. Geraghty uses silver nitrate solution up to as high as 5 per cent. for the treatment of pyelitis. More recently 1 per cent. **mercurochrome solutions** have been used successfully in the treatment of pyelitis. The advantage of the latter solution is that it is more penetrating and less irritating than the silver nitrate solution, and at least equally as effective and perhaps more effective as a bactericidal agent. The two drugs should be used interchangeably, being substituted the one for the other if the desired result is not obtained as rapidly as one would expect. If the precaution is taken to measure the pelvic capacity before the introduction of the solution, pain and kidney colic will be most often avoided. The treatment is carried out as far as possible about every four or seven days, and continued not only until the urine is clear and free from pus and microörganisms microscopically, but until sterile cultures are obtained. Negative urinary findings, both microscopically and culturally, must be repeated a number of times before the case can be discharged as cured.

TREATMENT OF CHILDREN.—Some little modification of this plan of treatment should be followed in the treating of pyelitis in children. The strength of the silver nitrate or mercurochrome solution should be about one-half the strength used for adults, and the amounts used should vary from 1 to 4 c. c., depending upon the size and age of the child. Until recently the possibility of treating children by **cystoscopic methods** was not sufficiently appreciated. This has been due to the fact that the family physician and pediatrician consider instrumentation in small children impracticable on account of the caliber of the urethra. We now have available cystoscopes, which will allow easy treatment in female children, with the exception of very young babies. In young boys, however, a perineal section would first be necessary. Such instrumental treatment may be justifiable, if the patients are the subjects of a persistent infection that is sapping their vitality and causing invalidism.

Indirect Method of Treatment.—The above outlined treatment may be considered under the head of direct method of treatment, but sometimes more important and necessary than the direct method of treatment is the indirect or accessory method of treatment. A careful history and physical examination should be made of the patient's entire body. X-rays of the teeth should be made, and infected tonsils removed. A careful examination of the gastro-intestinal tract is most important. The relationship between chronic constipation and other bowel conditions in the production of pyelitis has already been pointed out. The author has seen patients cured of recurrent attacks of pyelitis by the simple method of preventing chronic constipation. Various rectal conditions are undoubtedly important exciting factors in causing or keeping up colon bacillus pyelitis. These rectal conditions, such as fistulæ, fissures, hemorrhoids, should receive adequate treatment. A very common cause for the persistence of pyelitis, even after the most direct treatment, both local and internal, is the failure to recognize the important connection between infection in the prostate and seminal vesicles and pyelitis. If this fact is recognized, and the infection in the prostate and seminal vesicles is relieved by regular and systematic massage of both these organs and by irrigations, not only is the cure by the direct method hastened and achieved, but very often relapses and reinfections are prevented. Similarly, attention should be given to certain lesions in the pelvic organs of females, which are undoubtedly provocative of pyelitis. **Antiseptic douches** should be recommended, and various surgical procedures carried out, if pathological conditions in the female generative organs are accounted for, such as cystocele, rectocele, fibroid of the uterus, etc.

Treatment During Pregnancy.—There is a more important group of cases to be considered from the standpoint of treatment, namely, pyelitis that occurs during pregnancy or the puerperium. Three methods of treatment have been advised for this condition of pregnancy, namely: (*a*) Emptying of the uterus; (*b*) surgical removal of kidney; and (*c*) pelvic lavage. The first two methods are too radical, and should be rarely if ever considered. The author has treated a number of cases of pyelitis of pregnancy in which the patients were highly toxic, and where interferences, such as the termination of pregancy, or surgical interference upon the kidney, seemed necessary, yet he succeeded by **pelvic lavage** in not only relieving the patients of their symptoms but in permitting pregnancy to extend to the normal period. If conscientious and prolonged treatment of the pyelitis of pregnancy by pelvic lavage and other methods of treatment fail, and the patient is getting progressively worse, then consideration of the above-named surgical interventions may be in order.

Selection of Cases for Treatment.—It is obvious that before resorting to treatment for pyelitis in the above-named manner, organic disease of the urinary tract must be eliminated by careful urological study. It will be impossible to cure cases of pyelitis by lavage, etc., if there exists as the provocative factor organic lesions of the urinary tract which call for surgical treatment. It is also well to remember that certain cases of colon bacillus infection leading to the diagnosis of pyelitis may mask the presence of renal tuberculosis, and that every case of pyelitis should not only have a careful, microscopic study for the tubercle bacillus made, but inoculation experiments in the guinea pig are also necessary. The author recently had a case in which the patient had marked pyuria, with the colon bacillus present from the right kidney, and in which the negative results were obtained after careful microscopical study to demonstrate the tubercle bacillus. The patient had more than a normal function in this kidney, but inoculation experiments proved the condition to be tuberculosis. More important than the above was the knowledge obtained after further study, of the complete absence of the opposite kidney. In concluding consideration of the treatment of pyelitis, one must recognize that any form of treatment will at some time fail to achieve a cure. If the patient is suffering with an advanced form of pyelonephritis, internal treatment or vaccine therapy will fail. Pelvic lavage will also fail, because the infection is so generally disseminated not only through the pelvis, but the medulla and cortex of the kidney, that the silver nitrate solutions do not come into contact with the infective foci. However, the cure of chronic pyelitis can be obtained in about 60 or 70 per cent. of cases by the methods of treatment outlined. In certain cases of pyelitis or pyelonephritis of this advanced type, even though the patients cannot be finally discharged with urine sterile and free from pus, their well-being can be markedly improved and their lives prolonged.

Pathology.—The changes exhibited by the pelvis of the kidney, the seat of infection, may be designated as catarrhal, suppurative, hemorrhagic, membranous, and gangrenous. In the catarrhal variety, the mucous membrane becomes congested and is covered with a thin layer of pus or mucopus. If the inflammation becomes more extensive and ecchymotic areas develop, the term hemorrhagic is applicable. In the suppurative variety, the pelvis contains free pus, there is an imflammatory thickening of the pelvic walls, the pelvis becomes distorted, and ulceration occurs on its surface. Some pouching of the pelvis may occur sufficient to allow an accumulation of pus like the "bas fond" of the bladder seen in prostatic hypertrophy. This pus accumulation, plus the swelling of the mucous membrane, may cause sufficient encroachment upon the caliber of the ureteropelvic juncture to close it.

The membranous type is that form of pyelitis in which the pelvis is covered by a membrane made up of shreds of fibrin and bacteria, giving the surface the appearance of a diphtheritic membrane. Areas of ulceration or gangrene may be noted, either localized or general. There is also some change to be noted in the ureter as a rule, although in some cases it may show no changes whatever. The ureter change may vary in its degree of involvement. It may be dilated or hypertrophied. Indeed, all the changes described as occurring in the pelvis may be noted in the ureter. The practical significance of this is that in treating pyelitis by pelvic lavage, the catheter should not be introduced too far up into the ureter before making injection in order to secure medication of the ureter itself. In cases where the condition is more of a pyelonephritis than a pyelitis, in addition to changes noted in the pelvis, there are changes to be noted in the kidney. The kidney becomes small and dense, and shows a lobulated surface with an adherent capsule, and perhaps a small number of cysts containing serum or seropurulent substance. The chief changes are noted in the cortex. The latter may show fibrous tissue degeneration, containing lobules of fat. There may be nothing abnormal in the pyramids. Histological section reveals an infiltration of the stroma, with fibrous and fatty tissue which by their contraction cause obliteration of both tubules and glomeruli. This interstitial fibrosis is irregularly distributed, and where sclerosis is not present, the secretory epithelium tends to undergo compensatory hypertrophy.

PYONEPHROSIS

Definition.—Pyonephrosis may be defined as an accumulation of pus in the kidney pelvis or parenchyma. It ordinarily is impossible to draw sharp lines of distinction between the various forms of kidney infection. The distinction is arbitrarily made and for the convenience of description. For example, we often have the sequence of pyelitis, then pyelonephritis, and subsequently pyonephrosis. In the type of cases described as pyonephrosis, there is always associated a pyelonephritis, unless the pathological process has extended to such an extent that there is an entire destruction of the kidney parenchyma by the suppurative process, until the kidney is represented by a mere pus sac.

Etiology.—The same factors as well as the same organisms operative in the causation of pyelitis or pyelonephritis are active also in the production of the more serious kidney lesions. In addition to the above, there is always present in pyonephrosis some form of obstruction to the urinary outflow. The obstructive lesion may be anywhere between the kidney pelvis and the urinary meatus. Its most common location is at the ureteropelvic juncture. If the obstruction leading to back pressure changes in the kidney pelvis or parenchyma are unattended by microbial infection, the condition of hydronephrosis develops (*q. v.*). Pyonephrosis may be then defined as an infected hydronephrosis. This is true, but it may also develop in a kidney secondary to a pyelitis or pyelonephritis in which there was not at any time present a hydronephrotic kidney. The former type of pyonephrosis is termed a primary pyonephrosis. The methods of invasion described under pyelitis apply to pyonephrosis. It is difficult to state just when a pyelonephritis is converted into a pyonephrosis. According to Kelly and Burnham, any pelvis which contains 30 c.c. or more of pus should certainly be classified as a pyonephrosis. The amount of pus which may be present in pyonephrosis varies from 30 c.c. to inordinate amounts, even up to as much as three quarts. These enormous pyonephrotic cases are seen mostly in the type of cases which primarily were hydronephrotic. In pyonephrosis secondary to a pyelitis or pyelonephritis, there is often noted a marked destruction of the kidney parenchyma, but only moderate dilatation of the kidney pelves.

Symptomatology.—The clinical picture of pyonephrosis is most variable and the symptomatology may vary from the one extreme of having an enormous pyonephrotic sac filled with purulent material without symptoms, to the other extreme of a relatively small pyonephrosis producing the most profound symptoms of sepsis. The variability of the symptomatology corresponds greatly to the heterogeneousness of the underlying pathological process. Pus in urine is about the only thing that is common to all open forms of pyonephrosis. It exists as long as there is communication between the kidney pelvis and bladder. It may cease temporarily or permanently—temporarily, if the obstruction occasioning it (*e. g.*, plug of inspissated pus, or stone at the ureteropelvic juncture) is removed, and permanently, if the obstruction persists, or if the kidney undergoes suppurative dissolution. The above characteristics have given rise to the terms open and closed pyonephroses. The asymptomatic type of pyonephrosis is most generally seen in the form of open pyonephrosis or where free drainage exists between the kidney pelvis and the urinary channel below. Should occlusion of the ureter take place, however, free drainage is interfered with, absorption of toxins follows, resulting in constitutional symptoms, such as fever, chills and sweats, weakness, anorexia, increased pulse rate, leukocytosis, etc. The latter symptoms, however, do not necessarily indicate a temporarily closed pyonephrosis. They may also be noted in open pyonephrosis, due to an active suppurative process and destruction going on within the kidney parenchyma. Again, closed pyonephrosis may occur without producing fever and its allied symptoms. The urine in a closed pyonephrosis clears up and remains cleared until the obstruction occasioning it is relieved, providing there is no permament focus elsewhere in the urinary tract. However, a large percentage of cases of pyonephrosis have at least an associated pyelitis of the opposite kidney. The next most prominent symptom of pyonephrosis is pain or tenderness in the renal region. This symptom, too, is variable and the reason therefore easily understood, if we are familiar with the pathology and the mechanical force which may be at work in pyonephrosis. The pain may be spontaneous or elicited only on deep pressure. As often as not pain is entirely absent, even after deep pressure over the kidney region. Usually, however, a feeling of heaviness or a dragging sensation is felt in the back over the kidney region, and accentuated after deep pressure is made. Furthermore, the patient may have the most violent paroxysms of pain exactly simulating renal colic due to occlusion of the ureter and damming back of the urine and pus into the kidney pelvis or parenchyma. Palpation of the kidney with the idea of feeling the tumor mass is most unreliable. The kidney may not be much increased in size, or it may be hidden behind the confines of the thorax, or the patient may be too stout or muscular. However, if the distended renal sac lies below the arch of the thorax and is quite large, or can be brought below the arch of the ribs by inspiration, it can usually be readily palpated. Vesical symptoms due to a concomitant disease of the bladder, prostate or urethra, owing to descending infection may be most pronounced. These symptoms and their manner of production have been sufficiently discussed under the heading of pyelitis (*q. v.*). Just as often, however, vesical symptoms will be entirely absent.

Diagnosis.—Ordinarily, the diagnosis of pyonephrosis is most easy, especially if the aids at the command of the modern urologist are made use of. If marked pyuria, pain on pressure and a tumor mass is felt in the renal region, the probability of pyonephrosis is great. However, by use of the cystoscope, ureter catheterization, renal functional tests, x-ray, and pyelography, the diagnosis is not only made certain, but much additional information is gained which aids both in enabling us to form the correct judgment concerning the proper treatment to be instituted, and in giving the right prognosis. By means of the cystoscope we learn the condition of the bladder interior, and what association direct or indirect it has in causing the symptoms. The ureter, catheter and renal functional tests, the phenolsulphonephthalein test, chromocystoscopy, urine-urea elimination, etc., enable us to not only determine the source of the pus in the pyonephrotic kidney, but the amount of renal destruction already present. Moreover, it enables us to learn the condition of the opposite kidney: *i. e.*, first, whether the kidney is present or not; second, whether or not it is a congenitally atrophic or infantile kidney; and third and more important, it enables us to learn whether or not it is also infected and to what extent, and if it could carry on the necessary bodily renal function if radical treatment, such as nephrectomy, were contemplated. By means of the x-ray we can learn of the presence of stones and their location, and determine their amount of responsibility for the pyonephrotic condition. By means of the wax tip bougie in the ureter, we might detect a stone in the ureter causing obstructive symptoms leading to pyonephrosis. By means of pyelography, we can learn the amount of dilatation of the kidney pelvis and the amount of kidney destruction already present. From what has been said, therefore, it is obvious that a pyonephrosis patient should always have the services of a urologist, without whom intelligent treatment and diagnosis may be impossible. Indeed, it should be a cardinal rule never to treat a patient for pyuria until every means has been employed to determine its exact source and significance.

Treatment.—The treatment of pyonephrosis may be divided into the mechanical and operative. By the mechanical method of treatment we allude to means of combating or alleviating the condition without the aid of the knife. By the operative method, we mean resort to the knife.

MECHANICAL METHOD OF TREATMENT.—Pyonephrosis, being a condition due to obstruction and infection, is **never benefited by medicinal treatment of any kind.** The treatment must necessarily be mechanical in nature and consists in **ureter catheterization** of the infected side or sides and the carrying out of **pelvic lavage** as already described in pyelitis. The treatment by pelvic lavage is slightly different than that of pyelitis on account of the difference in the pathology present, *viz.*, pyelitis indicates septic inflammation of the pelvis, whereas pyonephrosis refers to septic inflammation, plus sac formation in the kidney. This factor requires, therefore, in addition to introducing antiseptic substances into the kidney, the washing out of the infected residual urine in the kidney by a process of **irrigations** or even **permanent catheterization**, the ureter catheter being left in the kidney for several hours or even as long as eight hours. It is surprising, at times, how much relief a patient can receive by this method of treatment. Proper drainage is instituted, septic absorption stopped, kidney function improved, and the patients are made more comfortable and life is prolonged. The mechanical treatment, however, is never curative and should be resorted to only when contra-indications exist to the operative treatment.

CONTRA-INDICATIONS TO OPERATIVE TREATMENT.—These consist of the following: (1) Cases in which the disease is advanced and bilaterial; (2) cases in which the opposite kidney is absent or of the infantile type (congenitally atrophic kidney); (3) cases in which the disease is early and a large amount of secreting substance is present; and (4) cases complicating far-advanced pregnancy.

OPERATIVE METHOD OF TREATMENT.—The operative methods of treatment may be of three kinds: (1) **Nephrotomy**; (2) **nephrostomy**; and (3) **nephrectomy.** The selection of the proper form of operative intervention depends upon several factors, *e. g.*, the degree of illness of the patient. A very sick patient requiring radical operation whose vitality is low had better first undergo nephrotomy or kidney drainage under local anesthesia. Again, nephrotomy would be first indicated in a pyonephrotic kidney, if the condition of its mate has not been determined, or if its mate is also badly diseased. Nephrectomy, primarily, is always the operation of choice in pyonephrosis if the patient's physical condition warrants it, and if careful urological and laboratory examination reveals no contra-indications. The advantage of this operation is that it is followed by rapid and permanent recovery, and the avoidance of troublesome renal fistula which may require subsequent secondary nephrectomy.

Prognosis.—The outcome of the disease is variable. It is surprising at times how patients who have marked pyonephrosis remain in good physical condition for months or even years. More often, unless interference is instituted, death occurs from uremic sepsis. Rupture into the ureter, into a neighboring organ and into the perinephritic fat may occur, giving rise to perinephritic abscess (*q. v.*). As already mentioned, the contents of a pyonephrotic sac may undergo a sort of caseation and become aseptic (Keyes).

Pathology.—The pathological changes present in a pyonephrotic kidney vary and are modified by the type of preëxisting lesion of which it is the culmination. The kidney may be nothing but a thin or thick wall-sac filled with purulent fluid. Puncture of the sac will cause the exit of the purulent fluid, which is usually thick and creamy, having a very foul odor, particularly if the bacillus proteus or certain strains of the colon group are responsible for the infection. The sac itself may show little or no vestige of former kidney tissue. Ordinarily, however, the interior of the sac is composed of a number of compartments, communicating or noncommunicating, separated by kidney tissue, sometimes fairly normal looking in appearance; more often, the kidney parenchyma shows evidences of interstitial fibrosis. The pelvis varies in the amount of its distention as already described. Its mucous membrane has lost its normal pinkish appearance entirely and is replaced by granulation tissue. The exterior of the kidney often presents a lobulated appearance, somewhat like an infantile kidney and in some cases it is not only adherent to the perinephritic tissue, but has caused certain inflammatory reactive changes in this region. The fatty capsule may be replaced by fibrous tissue, or it may be thickened and intimately adherent to the sac. Stones either of primary or secondary origin may be found. The size, shape and number may vary within wide limits. The ureter in pyonephrosis may present a fairly normal appearance, except in those cases where the pyonephrosis was secondary to obstructive changes in the lower ureter tract, or secondary to pyelonephritis when changes characteristic of the latter will be noted and which already have been described. Perinephritic abscess may be associated with pyonephrosis and is due to the rupture of the abscess into the perinephritic tissue, or the direct extension of the infectious organisms by contiguity of tissue. Pyonephroses are described as open or closed, this being dependent upon whether or not there is a patency or closure at the ureteropelvic juncture allowing or preventing communication between the kidney and the bladder. The condition may be unilateral or bilateral. If bilateral, a condition in which both ureter regions are equally obstructed is present, *e. g.*, prostatic hypertrophy, stricture of the posterior urethra or vesical neck, congenital valve formation, etc. Rarely, the second kidney may become pyonephrotic by hematogenous extension from its pathological mate primarily diseased. Occasionally adhesions to neighboring organs take place and rupture into them occurs. Exceptionally the contents of a pyonephrotic sac undergo a sort of caseation and become aseptic (Keyes).

PERINEPHRITIC ABSCESS

(Perinephritis)

Definition.—This condition consists of an inflammation of the fibrous (fatty) capsule surrounding the kidney. Suppuration does not always occur.

Etiology.—Inflammation may be primary or secondary. In the primary, the most common etiological factors are (1) trauma; (2) infectious disease; and (3) "colds" and hematogenous infections. The secondary follows infections of the kidney, as pyelitis, pyonephrosis, renal calculi, tuberculosis of the kidney, pyelonephrosis, or ureteritis. The primary focus may be at some distant point as the appendix, uterus, or its adenexa, spleen, gall-bladder or liver, tuberculosis of the spine or ribs, following removal of prostate or operations on other parts of the genito-urinary tract. Frank Kidd, of London, states that from pathological findings many cases of perinephritis arise from a small bacterial infarct situated just beneath the true capsule of the kidney, coming primarily from the blood stream and containing as a rule the staphylococcus aureus as the offending organism. It slowly burrows its way through the true into the fatty capsule, gradually digests this and is unnoticed until a large abscess is formed with its accompanying symptoms.

AGE.—It usually occurs in middle life, although extremes have been noted. It is generally on the right side and is more common in males. It may be bilateral or multiple when due to kidney disease.

Symptomatology.—The symptoms vary greatly depending upon onset, which may be acute or more commonly subacute. The location, as already stated, may be anterior, posterior, above or below the kidney. If the symptoms are acute and due to some kidney condition, you may obtain a history of this condition. The patient may have chills, temperature, prostration, and severe toxemia may be present. Urinalysis might be valuable. The blood-picture may show a septic condition unless due to tuberculosis. The abscesses, if situated, as is most common, behind the kidney, may first cause tenderness on palpation and later swelling in this region. If it progresses sufficiently, signs of pointing may appear, the skin taking on an edematous appearance, being reddened with a distinct mass formation. In this type, or in fact, the subacute as well, you find the patient favoring the affected side. If in bed, the thigh is adducted and flexed. If ambulatory, a limp is present. When the abscess follows any acute abdominal condition, as appendicitis, etc., the symptoms are masked by it. If the abscess has burrowed its way to the pleural cavity and formed a pneumopyothorax, the first symptoms which may appear are shortness of breath, cough, and dyspnea. Lung abscess may form, rupture and evacuate itself through the bronchus, causing a disappearance of most of the symptoms. Respiratory movements do not affect the abscess. It may also rupture into the kidney itself, ureter or bladder, confining symptoms to the genito-urinary tract; or into the colon and if so, pus in large quantities is found in the stools. Rupture into the peritoneal cavity may also happen, but this is rare. Tympany is present over the abdomen, but dullness is elicited over the lumbar region and does not change its position with that of patient. Pain varies in intensity and distribution according to the size of the abscess and its pressure on the surrounding nerves. It may radiate down to the genitalia or the thigh, or be confined to the lumbar region or abdomen.

TEMPERATURE.—The patient usually shows the septic type, but almost any type of chart may be obtained. Leukocytosis, unless the abscess is tubercular, is always present. Gastro-intestinal upset may be present in both the acute and the chronic case.

Diagnosis.—First obtain complete and thorough history, which may bring to light some previous infection either in the kidney itself, or in some other part of the body. Cystoscopy, uretheral catheterization, repeated urinalyses, and functional tests and pyelography should be carried out when necessary. If the latter is not used, plain x-ray may be of value. If a mass is present in the lumbar region, aspiration or exploratory operation may be necessary to clear the diagnosis. The following conditions often require elimination: Myalgia or lumbago, true renal colic, tuberculosis of the spine, ribs, or hips, appendicitis, and other inflammatory conditions in the pelvis. In some kidney conditions, as acute suppurative nephritis, pyelitis, neoplasms, and pyonephrosis, diagnosis is not made until operation is performed.

Treatment.—This is entirely in the surgeon's hands. **Lumbar incision** when possible with free drainage should be made. If kidney function is good, do not disturb; if poor with good function on opposite side, **nephrectomy** can be carried out by the use of a blunt dissection. The only medicinal treatment to be considered is that of an expectant or supportive nature.

Prognosis.—If the diagnosis is promptly made, and abscess points either in the iliac or the lumbar region, and thorough drainage is immediately carried out, the prognosis is very good. If rupture takes place into the pleura, it is grave. When rupture occurs into the kidney, ureters, bladder, or colon, the prognosis is influenced by the amount of damage done. If the abscess becomes encysted, complete recovery takes place.

Pathology.—Abscesses may be single or multiple. The fatty capsule is replaced by inflammatory tissue in the acute, and connective tissue in the chronic. The tissue varies very much in thickness. On cross section, it usually shows the presence of edema; what remains of the fatty capsule is infiltrated with connective tissues, and if the condition has been going on long enough the whole is replaced by cicatricial tissue. The position of the abscess may be in front, below or behind the kidney, the latter being the usual site. Depending upon its position, it finally dissects or burrows its way to the exterior, pleura, lungs, or bronchus, or evacuates itself into the intestines, kidney, bladder, or some other organ or part of the pelvis. The retrorenal abscess as a rule opens or makes its appearance at Petit's triangle. This, of course, aids the surgeon as well as the patient, the former in his diagnosis and treatment, the latter as far the prognosis is concerned. Other points where this type may find its way are the iliac fossæ, thigh and groin, or it may travel upward into the pleural cavity. Abscesses which have their primary focus in the kidney may be multiple. As a rule the abscess is single and of large size before operated upon, containing as much as a liter (2.11 pints) of pus, which may be odorless. This, of course, depends upon the organism causing the condition. Occasionally at operation there is profuse hemorrhage. When the abscess is primary, or from some distant focus, the kidney itself may show an amyloid degeneration. Martin-Thomas-Moorhead claim that 4 per cent. of recorded cases reach the pelvis postperitoneally and open either into the rectum, vagina, urethra, or bladder. Also 6 cases on record ruptured into the colon, 4 of which recovered. In Fisher's 94 cases, 24 per cent. affected the pleura, 20 per cent. the lungs, and 6 per cent. the pericardium.

HYDRONEPHROSIS

(Uronephrosis, Sackmiere (Kuster) Cystonephrosis, Nephrectasis, Renal Distention)

Definition.—Hydronephrosis is a dilatation of the renal pelvis, calyces or parenchyma substance, one or all, caused by a damming backward of aseptic urine, due to an obstructive influence somewhere along the urinary tract.

Etiology.—Anything which prevents the urinary outflow from the kidney in a normal manner may result in the formation of a hydronephrosis. In reality, it is a symptom and not a malady, an effect and not a cause. The cause is always something obstructive in nature, and may lie within or without the urinary channel, at any point between the urinary meatus and the ureteropelvic juncture. To produce a hydronephrosis, however, the obstruction must have certain forms or characteristics. *e. g.*, complete, total, long-continued or permanent obstruction will not produce a hydronephrosis, but a renal atrophy. If the obstruction is complete, only if it is short-lived and oft-repeated will it cause the lesion: if the obstruction is partial it must be long-continued, oft-repeated or permanent in order to cause hydronephrosis. The nearer the obstruction is to the renal pelvis, the sooner will hydronephrotic conditions manifest themselves, *e. g.*, a stricture or calculus at the ureteropelvic juncture will produce the lesion much more quickly than a stricture or stone in the urethra. In order to appreciate the rationale of the above statements concerning hydronephrosis a few words concerning the renal pelvis will be helpful. The renal pelvis is a funnel-like dilatation of the upper end of the ureter, designed not to act as a urinary reservoir like the bladder, but to receive the urine from the various calyces and allow its easy passage into the bladder via the ureter. Under ordinary circumstances the urination is easy and unimpeded and even if a certain amount of obstruction from whatever cause should develop, hydronephrosis would not occur providing the amount of urine excreted did not exceed in amount that capable of trickling through the obstructive portion without causing a back-flow. When the amount of urine excreted by the kidney becomes greater than that which is allowed to flow beyond the obstructive region, dilatation, beginning first just behind the obstructive area, occurs and gradually extends upward to the kidney pelvis; then the calyces and finally the kidney substance will become involved in the process. Generally speaking the causes of hydronephrosis are congenital and acquired.

Congenital Hydronephrosis.—Under this heading are grouped defects, mostly of the ureters, that are of congenital origin. Some of these ureteral anomalies that are responsible for the production of hydronephrotic lesions are the following: absence of the ureters, single or multiple ureters, abnormal position of the orifices, bends or twists, narrowing and valves of the ureters and imperforate ureters. There may also be included narrowing caused by the pressure exercised upon the renal pelvis or ureter by abnormally placed branches of the renal blood-vessels. There is practically no congenital defect disturbing the bladder that gives rise to hydronephrosis; and in the urethra, the only congenital anomaly that may secondarily cause the formation of a hydronephrosis is the so-called congenital valve formation of the posterior urethra. Phimosis, and in rare instances, urethral stricture, may cause renal distention.

ACQUIRED HYDRONEPHROSIS.—The cause of acquired hydronephrosis may be found in any portion of the urinary tract, and the etiological factor may act from within or without.

URETERAL OBSTRUCTION.—The obstructions from within the ureter causing hydronephrosis are the following: stricture (most commonly at the ureteropelvic juncture), stone, tumor, or foreign body in the ureter. Pressure from without the ureter may rarely cause hydronephrosis, *e. g.*, pelvic growth, kinking or twisting of the ureter from abnormal renal mobility (nephroptosis), inflammatory adhesions, etc.

URETHRAL OBSTRUCTION.—This arises from enlarged prostate and stricture. These latter organic diseases accomplish their damage rather by infection than by distention. Inflammatory and ulcerative disease about the region of the urinary meatus may cause urethral obstruction.

THE FLUID.—The quantity of fluid in a hydronephrotic sac varies within wide limits. The normal pelvic capacity is about 7.5 c.c. with variation limits between 1 and 20 c.c. Hydronephrotic sacs have reached a capacity up to 5 or 6 gallons. Glass reported one case containing 30 gallons. The color and odor of the fluid is slight and of very low specific gravity. Urea, uric acid and other urinary solids may be greatly diminished or entirely absent. There is often found in the fluid some red blood-cells, desquamated epithelium, leukocytes, casts and albumin. There may be a slight associated catarrhal pyelonephritis which does not affect in any way the clinical aspects of the condition. A hydronephrotic kidney is prone to infection and when the latter occurs an infected hydronephrosis or pyonephrosis results.

Symptomatology.—The symptoms of hydronephrosis may be classified clinically into latent, intermittent, and persistent or fixed.

LATENT HYDRONEPHROSIS.—By latent is meant a hydronephrosis which exists without producing manifest symptoms or signs. It may be discovered postmortem, or during the routine of a complete urological examination.

INTERMITTENT HYDRONEPHROSIS.—In this type symptoms come irregularly and are characterized by severe attacks of pain in the side. The pain may exactly simulate renal colic. The intervals and frequency of the attacks vary. The pain after lasting several hours or days is suddenly relieved by the passage of a large quantity or urine. Oliguria is usually present during the stage of pain. During the attack the distended kidney may be felt completely filling the entire loin, although very severe attacks of intermittent hydronephrosis may be seen without evident tumor formation. After the attack, if a tumor has been present, it will be reduced in size or disappear entirely, to recur or become obvious at the next attack. Tenderness over the kidney region is often noted during the attacks. Prostration may be present but fever and leukocytosis are absent. The usual sequence in intermittent hydronephrosis is its transition into the fixed or permanent type. The tumor mass tends to maintain its size and the pain becomes more constant but less aggravated. If the condition is bilateral symptoms of uremia may develop.

Fixed or Permanent Hydronephrosis.—When the hydronephrosis is fixed or permanent, the patient may have remarkably few symptoms and enjoy a fair state of health. The patient usually gives a history of a slowly growing tumor in the region of the kidney, with a feeling of soreness or pain or a dragging sensation. The latter symptoms may be present before the tumor can be detected. The tumor grows very slowly. The urine passed is normal in amount and quality providing the condition is unilateral. In rare cases it may burst into the perinephritic space or the peritoneal cavity.

Diagnosis.—The one classical sign of hydronephrosis is a tumor in the loin. However, marked and well-formed bilateral hydronephrotic sacs may be present without evident tumor formations. From a therapeutic standpoint it is most important that the diagnosis be made before the development of a palpable tumor. With the employment of the modern urological aids at our command, in the vast majority of cases this ought to be easy; without them, extreme difficulty of diagnosis has often to be encountered. The conditions that may be confused with it are both renal and extrarenal. The extrarenal conditions that suggest hydronephrosis are the following: ovarian, pancreatic, mesentery cysts, encysted ascites, gall-bladder disease, appendicitis, and neoplasms of the liver and spleen. The renal condition that may simulate hydronephrosis, and with which it may be associated are renal stone, neoplasm, tuberculosis, polycystic kidney, hydatid cysts, ureteral strangulation (Dietl's crisis), pyonephrosis, perinephritic abscess, etc. The differential diagnosis of these many conditions from hydronephrosis is usually easy to the urologist and it will be necessary to enlist his aid not only in determining more accurately the diagnosis but other factors as well, such as the grade or extent of the hydronephrosis, the functional capacity resident therein, the condition of unilaterality or bilaterality, the presence and condition of the other kidney, should nephrectomy be contemplated, etc. The location and nature of the obstruction and other data must be sought for. On this account, it does not seem necessary to go deeply into the differential diagnosis between hydronephrosis and the many other conditions enumerated above. A hydronephrosis that has developed to the stage of palpable tumor formation presents certain characteristics that make its diagnosis strongly presumptive, even before the use of the urologist's armamentarium. These characteristics are dullness on percussion and movements corresponding to those of the diaphragm. If the tumor is of moderately large size, the colon lies in front of it, and percussion may reveal a tympanitic rather than a dull note. If the hydronephrosis is of large size, the colon and intestines are usually displaced to the side. Sometimes in thin-bellied people the lobulated character may be made out and fluctuation may be recognized. Pain is a variable symptom, which fact is easily understood from the study of the pathology of hydronephrosis, which has been sufficiently discussed under the heading of symptoms. The aids necessary in the diagnosis and intelligent treatment of hydronephrosis are (1) the cystoscope; (2) ureter catheterization; (3) renal functional tests; (4) x-ray; (5) pyelography; and (6) wax tip.

THE CYSTOSCOPE.—If a tumor is felt in the loin, it may be possible to diagnose hydronephrosis by means of cystoscopy by observing the ureteral orifices, especially if the patient has previously received an injection of indigocarmin or methylene-blue. The absence of urinary flow on one side, with active flow on the other may be determined; more frequent contractions during polyuria, fewer during the stage of oliguria can be determined. Intermittency or continuousness of flow is recognizable. The indigocarmin elimination, both from the standpoint of its time of output and intensity of color, may give one an idea of the relative functional capability of the kidneys. In the early stage of hydronephrosis, the cystoscope will not prove very helpful and the ureter catheter must be employed. This aid should always be made use of on account of the great and necessary information it enables us to obtain. By it we can learn the character of the urine from each side, the functional ability of each kidney—especially the urea elimination output—and the pelvic capacity of each kidney. A pelvic capacity of 30 c.c. is considered sufficient to diagnose hydronephrosis and a pelvic capacity of 150 c.c. is regarded as indicative of much destruction of kidney tissue. By means of the ordinary x-ray we can not gather much information concerning the diagnosis of hydronephrosis, unless stone is the obstructive factor responsible for it. However, by using the x-ray in conjunction with the injection through the ureter catheter into the kidney pelvis of certain shadow-casting substances (sodium bromid, sodium iodid, thorium, collargol, argyrol, etc.), the diagnosis in the vast majority of cases can be clinched. By it the shape, size, and position of the kidney may be determined and often the distinctive cause responsible for the hydronephrosis may be seen. This is called pyelography or urography. Its application makes the diagnosis not only certain, but in the majority of cases it also renders easy its differentiation from the many organic conditions that might simulate it. Renal functional tests are not only great diagnostic aids, but prognostic as well. As has already been mentioned, one cannot judge of the functional capacity of a hydronephrotic kidney after pyelography or even at the time of an exploratory operation, but the greatest aid in this regard is obtained by the renal excretory tests properly employed, particularly, the phenolsulphonephthalein test and the urea elimination test. By these same tests the condition of the other kidney also is obtained which aids not only our judgment as to proper procedure of treatment, but also enables us to give the right kind of prognosis. By means of the wax tip, we can often learn of the presence of a stone in the ureter, when the ordinary x-ray fails to reveal its presence. We thereby learn to know it as the causative factor of the hydronephrosis.

Treatment.—In the treatment of hydronephrosis certain important considerations ought to be kept continually in mind, *viz.*:

(1) The condition ought to be recognized as early as possible or before much damage to the kidney has been done.

(2) The discovery and removal of the obstruction is the most important element in the treatment.

(3) Never remove a hydronephrotic kidney unless thorough study from all standpoints indicates this as the method of choice.

Medicinal treatment is **valueless** in the treatment of hydronephrosis. Some form of **surgical** or **mechanical treatment** has to be employed, either for the purpose of relieving the obstruction or, when this is impracticable or impossible, of relieving the condition itself. Aspiration, except in doubtful cases for diagnostic purpose and then rarely, is mentioned only to be condemned. The **dilatation of the ureter** by the ureter catheter may occasionally relieve the condition. The **operative measures** for relief of the cause of hydronephrosis and the condition itself follow: stricture operations, prostatectomy, removal of bladder obstruction (tumor, stone, etc.), division of bands constricting the ureter or pelvis of kidney, removal of intra-ureteral obstructions (strictures, valves, calculus, etc.), ligature and section of aberrant renal vessels, plastic operations upon the ureter and pelvis, nephropexy, nephrotomy, nephrolithotomy, nephrectomy, etc. To discuss the indications for any of the above operative procedures would carry one too far into the domains of surgery.

Prognosis.—In bilateral hydronephrosis the prognosis is bad. In simple unilateral uncomplicated hydronephrosis the prognosis is good. Patients with well-developed single hydronephrosis may live many years and in comfort. Complications may develop,however, which may render the prognosis grave. Some of these are infection causing pyonephrosis, complete occlusion of the ureter by a calculus being arrested somewhere in its course, leading to pressure upon important neighboring organs, rupture into the peritoneal cavity (seldom) with resultant peritonitis. If the condition has been recognized early and the cause removed, cure may follow; but in the advanced cases the damage already done is irremediable. Spontaneous disappearance of hydronephrosis has been noted in 6 or 7 cases out of the 44 observed by Morris.

Pathology.—The effect of hydronephrosis upon the renal structure is dependent upon the character and duration of the obstructing influence. In the early stages the dilating effect is confined to the pelvis, but later on, if the causative influence is not removed, characteristic changes take place in the kidney substance proper. The dilated pelvis and kidney form an irregular, nodulated tumor mass varying in size from that of a normal kidney to an enormous tumor containing many pints of fluid. The hydronephrosis may be single or bilateral depending upon the location of the obstruction. Since the advent of ureteral catheterization, pelvic measurement and pyelography, many early cases of hydronephrosis are recognized in which the pathological changes involve only the pelvis or at most the calyces. The advantage of this is obvious, as it enables us to locate and remove the cause before irremediable damage to the kidney proper is done. The sequence of events in a hydronephrosis is as follows: **First** a dilatation of the kidney pelvis, to be followed shortly by flattening, then widening of the calyces. This causes increased pressure upon the intermediate medullary substance, resulting in pressure atrophy. The more resistant capsule and fibrous tissue septa resist the increased intrarenal pressure longer than the parenchymatous substance, causing the mass to assume the lobulated or nodular appearance above described. On section, the appearance of kidney interior varies. There is noticeable an apparent atrophy of the renal parenchyma. The pyramids are more involved and sooner attacked than the cortex in the thinning-out process. The multilocular cavities, separated by septa formed by the columns of Bertini, communicate freely. In the more advanced cases these latter also disappear by atrophy, so that we have nothing left but a big thin-walled sac in which no vestige of kidney tissue is macroscopically discernible. Usually, however, traces of the septa are visible and there are some remnants of secreting substance. The cells composing the latter undergo a compensatory hypertrophy. They grow to three or four times their normal size with a corresponding increase of their functional capabilities. This is not only interesting but of importance practically. One cannot judge of the functional capability of a hydronephrotic kidney by its microscopic appearance, no matter how serious it appears; and before sacrificing a hydronephrotic kidney by nephrectomy, renal functional tests should be previously performed. Furthermore, these kidneys have their functional capability increased after operation causing the release of pressure occasioned by the retained urine. The pelvis at its place of junction with the ureter may be much distorted. The ureter is usually open, but it may be closed. The opposite kidney, if it is not itself involved, will undergo a proportionate degree of compensatory hypertrophy.

KIDNEY AND URETERAL STONE

(Renal calculus, nephrolithiasis)

Definition.—Kidney and ureteral stone is the formation or development within the kidney of coalesced urinary salts or solids.

Etiology.—A large amount of work, study, and experimentation has been carried out by many different investigators with the idea of determining the exact etiology of stone formation, but the results are far from conclusive and are quite contradictory. There are certain general and local disturbances which have been described as provocative of stone.

Systemic or General Factors Concerned in Renal Calculus Formation.—Many factors of a systemic nature have been described as provocative of stone formation, but at most all that can be said concerning them is that they are predisposing, *e. g.*, the influence of diet.

Influence of Diet.—Sugar in the opinion of many is bad for patients suffering with a calculus or gouty diathesis, yet renal stone is extremely uncommon, according to Professor Harley, quoted by Watson and Cunningham, among women of the Turkish harems, who lead sedentary lives and consume great quantities of sugar and sweetmeats. Similarly, gout and calculus are extremely rare among the negroes of the South who during the sugar cane season consume great quantities of sugar and sweetmeats. Some claim the ingestion of meat and large quantities of other forms of nitrogenous foods and alcoholic drinks are provocative of stone. Contradicting this claim is the experience of surgeons, who see yearly thousands of calculus cases in certain natives of India who are not only abstainers from alcoholic drinks but are also vegetarians. At most, then, diet can be claimed as a predisposing factor in stone formation, and only in certain predisposed individuals. Other general predisposing factors may be grouped under the heading of metabolic disturbances affecting the gastro-intestinal apparatus, *e. g.*, the stomach, liver, intestine, pancreas; the organs concerned in eliminating waste products, *e. g.*, the lungs, skin, lower intestines and kidneys; defective oxygenation; insufficient muscular activity; etc. Heredity and climate have also been claimed as factors.

LOCAL CONDITIONS CONCERNED IN STONE FORMATION.—The most accepted theory concerning the effect of local conditions upon stone formation is that advanced by Rainey over forty years ago. In brief Rainey's theory is that before formation of stone takes place, a colloid material formation acting as a nucleus develops, about which crystalline substance tends to coalesce and take spheroid form. This colloid substance is said to be the product of, or associated with a desquamative condition of the epithelium of the renal pelvis and calyces, etc. The weakness of this theory has been pointed out by observations which tend to show that this colloid substance exists under normal conditions. Shattuck, quoted by Cabot, says, "It has commonly been supposed that some adventitous substance is necessary to serve as a starting point, such as shed epithelium, mucus, blood-clot, bacterial colonies, or foreign bodies strictly so called, that is, introduced from without. It is one of the established facts in regard to crystallization that the genesis of crystals as distinguished from their growth takes place only in supersaturated or labile solutions. In the production of such no foreign material is necessary. It will be evident from this that in the formation of uric acid sediments as well as of calculi, the secretion of a urine supersaturated in uric acid is necessary before crystallization can occur. The presence of shed epithelium, etc., is not necessary to start it in the supersaturated fluid, and it would be quite unable to do so in the urine which was simply saturated." Cabot believes the formation of stone is largely dependent upon certain mechanical factors. It is a well-known and established fact that if a foreign body, *e. g.*, a piece of catheter, silk suture material, or a piece of stone, remains in the urinary tract to act as a nucleus, additions of urinary salts thereon will invariably occur, resulting in definite stone formation, even though the urine will be normal in every respect and there is not present supersaturation. It is also a well-known fact that crystals (sand) of sufficient size to act as a nucleus often form in the urine without stone formation. However, if the crystals are caught and retained somewhere in the urinary tract, even for a short time, stone formation may result.

This theory of Cabot's seems very plausible, and makes more easily understandable the element of heredity as a factor in stone formation.

Stones are described as primary and secondary. By primary stone is understood a stone which develops somewhere in the urinary tract free from infection. By secondary stone is understood a stone that develops somewhere in the urinary tract the seat of a morbid process, *e. g.*, pyelitis, pyelonephritis, or pyonephrosis. The type of primary stones that form in aseptic kidneys are the urate, oxalate, and cystin. Very often as a result of infection or other causes, a primary stone may have secondary deposits thereon of phosphatic or other salts, and give rise to a mixed or a laminated stone. Cabot objects to the theory of secondary stones forming as a result of infection. He admits that infection in the urinary tract is an important factor in influencing the kind of stone that forms, but does not cause its formation. He cites the well-known experience of urinary infection extending over a period of many years without stone formation. Infection by certain organisms, such as the pyogenic cocci, results in the formation of alkaline urine. In such urine only phosphatic calculi develop, whereas in acid urine, uric acid, urate and oxalate calculi form. The variability in the composition may occur from time to time and affect coincidentally the composition of the urine. For example, as a result of some excretory or metabolic perversion, a uric acid stone forms; the irritation resulting from it sets up an infection with alkaline urine; phosphatic salts are now deposited upon the primary uric acid stone. Subsequently, the infection clears up, the urine returns to the normal acid reaction, and the phosphatic salts are replaced by deposits of other urinary salts like or unlike the original composition. This explains the reason for the laminated stone so often encountered.

CHEMICAL COMPOSITION.—There is much discussion in the literature concerning the most frequent type of kidney stone encountered, some claiming the uric acid and uratic stones are the commonest variety, whereas others maintain that the oxalate of calcium is the type most often seen. Statistics show that on the European continent, the uric acid and urate stones predominate, whereas in this country, the oxalate of calcium is the most common. Phosphatic stones, which are composed of the phosphates of calcium, ammonium, and magnesium are the next most common. Stones of xanthin, cystin, and indigo are rare. Stones, too, may be divided into the acid, the alkaline, and the mixed types. The acid stones are all of the above except the phosphatic variety and the mixed type is one composed of two or more of the different urinary constituents. The method and reason for the formation of the latter has already been explained. Stones consisting purely and entirely of any one urinary constituent are the exception rather than the rule.

PHYSICAL CHARACTERISTICS OF CALCULI.—Renal stones vary considerably as regards their color, consistency, surface and contour. The hardest calculi and the most irregular in type are the oxalates. They are usually dark and even black in color, having knob-like projections, on which account they are often alluded to as jackstones or mulberry calculi. Uric acid calculi are usually soft, smooth, oval and rounded, and the color may vary from red to brown. Uratic calculi are harder than the uric acid calculi but not as hard as the oxylate. They are smooth, round or oval in shape, and the color is usually yellowish. Phosphatic calculi are chalk-like or greyish; they may be very brittle or hard, or they may be smooth but more often irregular.

As to number, they may be single or the kidney may contain as many as a thousand stones. Their size may vary from minute concretions referred to as "sand" up to a weight of 1½ pounds (Shield's case). If the stone is single and not subjected to peculiar pressure, etc., the shape is usually round or oval. If the stones are multiple, they are apt to be faceted; certainly so, if they are in contact with each other. In operating for stone, if a faceted one is found, it indicates the existence of one or more others. If the calculus lies in the pelvis and sends branches into the calyces, the so-called stag-horn calculus is formed. Kraft, quoted by Keyes, found renal calculi forty times in 2,953 autopsies. Both kidneys were affected fifteen times. Males are more frequently affected than females. In 188 cases with renal calculus, Morris gives the ages as follows:

Under 10 years	1
Between 10 and 15 years	10
Between 15 and 20 years	20
Between 20 and 30 years	54
Between 30 and 40 years	50
Between 40 and 50 years	34
Between 50 and 60 years	17
Between 60 and 65 years	2

Symptomatology.—Pain.—The symptomatology of kidney stone varies within wide extremes. The symptoms are not so much dependent upon the number and size of the stones as upon their location. One may see bilateral multiple calculi of unusual size presenting no symptoms and their presence revealed by accident only while examining the patient for insurance, or after x-ray study has been carried out as a part of a routine examination. On the other hand, a small pea-sized stone, shell-like in character, causing blocking at the ureteropelvic juncture may give rise to the most distressing and agonizing symptoms. Stones of the former variety are referred to as silent stones. The symptoms of the latter type are referred to as renal colic. When renal stone is confined to the region of the kidney substance, there may be no symptoms whatever (silent stone), but in about 80 per cent. of the cases a pain, dull in type and referred to the region of the kidney, will be present. The patients will refer to a feeling of soreness in the back, which may be aggravated by jolting or jumping, or there may be some costovertebral tenderness on pressure. When the stone leaves the kidneys and enters the pelvis and becomes blocked in the ureteropelvic juncture or some other portion of the ureteral canal, symptoms are produced of renal colic, which occurs at some time or other in about one-half of all cases of kidney stone. It is most often but not always itself typical. Perhaps the best description of kidney colic is that of Montaigne (Essays, Book III, 13), who was for many years a sufferer: "Thou are seen to sweat with pain, to look pale and red, to tremble, to vomit well nigh to blood, to suffer strange contortions and convulsions, by starts to let tears drop from thine eyes, to urine thick, black, and frightful water, or to have it suppressed by some sharp and craggy stone, that cruelly pricks and tears thee." The pain when typical, comes on suddenly and without warning, at any time in the day or night, and independent of exercise, exertion, or any other provocative factor. The pain is sharp, agonizing, felt in the back rather than anteriorly, although it is surprising what a large number of cases are mistakenly diagnosed as appendicitis or biliary colic. The pain may be localized, but more often it radiates down the course of the ureter and is felt ultimately in the region of the bladder, symphysis, penis or testicle. It may produce pains exactly simulating sciatica, or the pains may be felt even in the legs or toes. Rarely the pain radiates upward toward the shoulder, and if the latter is on the right side, the diagnosis of biliary colic is more often made, whereas if the radiating pain is felt on the left side, angina pectoris is thought of. The duration of an attack varies from a momentary flash to many days of constant suffering that even morphia is powerless to calm. In some of the attacks the pain may disappear after a short time, but nausea and vomiting may persist for days or the two symptoms may be associated.

One of the striking features of renal colic, however, and a point which has much diagnostic significance, is the absence of constitutional symptoms during the attack. There is no chill or fever present, unless there is concomitant infection, and the pulse is normal in rate and volume. Urinary symptoms may or may not be present, but a consideration of the urine is of the greatest diagnostic importance. Oliguria may be present during the attack, polyuria immediately after. Urgency and vesical irritability have been described as symptoms during renal colic. But the most important urinary finding is the presence of red blood-cells in the urine. There is nothing in the opinion of the author that is more pathognomonic of renal colic than blood in the urine. It may be profuse or so slight that it is revealed only after careful microscopic examination. The author has eliminated many supposed cases of renal colic by the failure to find microscopic blood in the urine and conversely, one should hesitate to diagnose a case of appendicitis or biliary colic if the microscopic examination of the urine reveals red blood-cells. Perhaps from 15 to 20 per cent. of kidney colic cases give a previous history of an appendectomy which failed to relieve the symptoms. Albuminuria is frequently present with renal calculus, and, if infection is present, pyuria is also noted as well as cocci or bacilli. Between the attacks of renal colic, the urine may be entirely negative (15 per cent. of cases). However, in the vast majority of cases, albuminuria, pyuria or hematuria, one or all, will be found constantly present. The periods between the attacks vary greatly. A patient may have one and the only attack, or they may recur with considerable frequency.

Diagnosis.—Often the diagnosis of stone is most easy. At other times it is most difficult and one must be prepared to differentiate from it not only every other kind of renal condition, such as infections of all sorts, mechanical or obstructive conditions, neoplasms, etc., but almost every disease that gives rise to intra-abdominal symptoms. Illustrations of some of the most common are the following: Ulcerative disease involving the stomach and duodenum, appendicitis, disease of the gall-bladder and its ducts, pathological conditions of the female generative tract, lesions of the spine, including those of the sacro-iliac joint, and disease of the central nervous system, particularly locomotor ataxia. It is surprising how often patients with renal stone have undergone previous surgical operations for removal of the appendix, ovarian or gall-bladder disease and how often the gastric crises of tabes are diagnosed only after the patients have failed to get relief following operative intervention. The above should emphasize the great importance of thoroughly investigating every intra-abdominal condition from all standpoints before deciding upon operative intervention. For example, if a simple microscopic examination of the urine were made in every case of abdominal pain, many unnecessary appendix operations would be avoided. About 20 per cent. of the patients who have had kidney stones removed by the author have had previous operations for appendicitis, gall-bladder disease, etc., done without benefit. In the vast majority of the cases this error would have been avoided if only a careful examination of the urine had been made. It has been the author's experience that in almost every case of renal colic, at least microscopic, if not macroscopic blood, will be found in the urine. This same information has been of value conversely, *viz.*, a number of intra-abdominal conditions diagnosed as renal stone have been proven erroneous by fuller study when a microscopic examination of the urine failed to reveal red blood-cells. It is important in this connection to remember that if the suspected case is in a female, the urinary examination can have significance only if the specimen is obtained by careful catheterization. If infection is associated with the stone, pus in the urine, varying with the amount of infection, is present. Albuminuria, also variable in amount, is usually present. Casts are the exception rather than the rule. Exfoliated epithelium may be noted and crystals of the type of stone present are not rare, and when present highly suggestive. Next in importance in the diagnosis of kidney stone is the x-ray. With the improved x-ray methods, it is possible to detect stones in the kidney in about 95 per cent. of the cases. On the other hand, it is well to remember that the x-ray, if depended upon alone, can lead one into serious error. The latter statement needs greater emphasis when discussion of the diagnosis of ureter stone by the x-ray is considered. Various conditions, such as calcified lymph glands, phleboliths in the pelvic veins, calcified spots in the pelvic ligaments, concretions in the appendix, moles on the back, etc., may give rise to shadows suggestive of stone. On this account, it is a good rule never to diagnose renal calculus from the x-ray picture alone but only when supported by additional diagnostic data. Negative x-ray findings, even though stone is present, may be due to several factors, such as a bowel overdistended with gas and feces (avoided by previous 24-28 hour catharsis), obesity, poor x-ray technic, and the composition of the stone. Oxalate and phosphatic stones show well with

the x-ray because they are rich in lime salts, while pure uric acid and cystin stones may fail to show because they are soft and have a density comparable to the body tissues. Fortunately, however, cystin stones are extremely rare and uric acid stone is usually mixed with a certain percentage of oxalates or is covered with phosphatic salts. Having diagnosed stone, *e. g.*, by the symptoms of renal colic, urine examination and the x-ray, other essential data of great importance must now be determined. These data are (1) the number, position, size and distribution of the stones; (2) the presence or absence of infection; (3) the functional condition not only of the affected kidney, but of the opposite kidney as well; and (4) the general physical condition of the patient.

The former three requisites are obtained by use of the x-ray, cystoscopy, ureter catheterization, wax tip bougie, bismuth bougie, pyelography, and renal functional tests (phenolsulphonephthalein, chromocystoscopy, urine-urea estimation, etc.). These methods have been sufficiently discussed in other chapters to make their repetition unnecessary. The general physical condition of the patient is obtained only after careful physical examination of the cardiorespiratory apparatus, etc., in order to obtain information which will not only afford prognostic aid, but enable us many times to exercise the proper methods of treatment and give us the correct judgment in the individual case.

Treatment.—The character of the treatment of renal calculus depends upon various factors, *viz.:* (1) Whether we have seen the patient for the first time during an attack of renal colic; (2) whether the stones are unilateral or bilateral; (3) whether infection is present or absent; (4) whether the stones are so small that they might pass spontaneously or with the aid of manipulative measures; and (5) whether the stones are too large to pass.

TREATMENT OF RENAL COLIC.—If the patient is seen during an attack of renal colic, immediate and prompt relief should be given. If the attack is not too severe and the patient's condition good, a hot **sitz-bath, hot water bottle,** or **turpentine stupes** applied to the kidney region may prove beneficial. But the best treatment for this condition is the **hypodermic injection of morphin,** given with a generous hand, till the condition is relieved. Massage over the region of the ureter in a downward direction has been of doubtful utility in the author's experience. The use of the **ureter catheter** to and beyond the stone with injections of **olive oil** and **cocain** around it, may displace the stone, facilitate its passage and relieve the ureter spasm, after the suggestion of Crowell. The symptoms may be so severe and distressing that the administration of **chloroform** or **ether** may be necessary. The use of the latter may not only afford temporary relief to the agonizing patient, but the author has seen it allow passage of the stone spontaneously by releasing the tight spasm of the ureter around the stone. **Papaverin** has been recommended by Macht as of great value, because it is supposed to have both an anodyne as well as a stimulative effect upon the muscular walls of the ureter. Following an attack the patient should be put upon **urinary antiseptics** for a few days and encouraged to **drink abundantly of water.** In the meantime study of the case should be carried out. During the attack of renal colic,

the possibility of anuria should be thought of and watched for. After the attack, the urine should not only be voided in a chamber, but preferably strained through gauze; otherwise the stone may be passed and missed. Some idea of how the stone is behaving may at times be gleaned by the character of the symptoms. If, however, the pain and tenderness, beginning in the loin, gradually works down the abdomen and suddenly ceases, it may be assumed that the stone has passed into the bladder, whence it can be expected as an ingredient of some urination during the next few days, or it may be revealed to the eye during a cystoscopic examination. Having rid the patient of his colic has not cured him of his stone, but for an intelligent future handling of his case, an x-ray study should be carried out, because, if it is not done, the patient may be exposed to all dangers and complications of neglected renal stone.

TREATMENT OF KIDNEY STONES—UNILATERAL.—In the consideration of this phase of the subject, items 2, 3, and 5 (see page 718) may be considered. If a kidney stone is unilateral, free of or associated with infection, and too large to pass spontaneously, providing there is no serious contraindication, *e. g.*, a serious heart or lung condition which would prevent the patient from undergoing the ordeal of a major surgical operation, **removal of the stone by means of the scalpel** should be the only course considered. The reasons for this position are the following: (1) If infection is not present, it is most likely to occur sooner or later, with such consequent destruction of kidney tissue that it has no functional value; (2) the dangers then to the body of an infected kidney (pus bag) have already been enumerated; (3) operation prevents these occurrences; and (4) operation prevents the occurrence of colic and the possibility of the stone being a source of constant discomfort or worry to the patient.

The type of operation will vary with conditions present. If the stone is associated with a serious destruction of the kidney so that it has little or no functional value, **nephrectomy** is the operation of choice; otherwise **nephrotomy** is indicated.

TREATMENT OF SMALL STONE—UNILATERAL.—In this type of stone, judgment concerning the proper course to pursue may be difficult. It is surprising at times, how large a stone may really pass down the lumen of the ureter and be voided. If the stone is in a kidney whose urine is uninfected and is causing no symptoms, it may be best to let it alone providing its size is not 2 cm. (.8 in.) or more in width. A larger stone than this will hardly ever pass spontaneously. The plan to pursue in this type of case will be to have the patient's urine kept antiseptic by **urotropin** internally and **forced water by mouth** and to **roentgenograph the stone** at periodic intervals. If the stone is not showing any increase in size at these times and watching the patient's urine gives negative results, matters can be left to remain as they are. Efforts to dislodge the stone by injections through the ureter catheter of **cocainized olive oil** is a procedure worthy of trial. Even if the patient develops occasional attacks of colic, one can still pursue the policy of watchful waiting, as the author has seen stones, giving rise to periodic attacks of colic for several months, finally pass into the bladder. If however, the attacks of colic are very severe and oft-recurring, and the x-ray shows the stone immobile, operative intervention may be left to the decision of the patient. If the x-ray gives evidence that the stone is increasing in size or if the urine becomes infected, **operative intervention** before further damage is done had better be carried out.

TREATMENT OF STONES IN BOTH KIDNEYS.—There are many problems and different situations which it may be necessary to consider in a patient who is subject of bilateral renal calculi. If both kidneys are extensively diseased and the patient has not much pain and suffering, it may be the better part of wisdom not to subject him to the danger of an operation. If the kidneys are uninfected and in good functional condition, **operation** better be carried out as a preventive measure. If one kidney is in good condition and the other kidney functionless or nearly so, operation on the healthier kidney should be carried out. Nothing will be gained by working upon a useless organ, but conservation of the healthier kidney is essential. Many other more or less similar propositions will come in treating cases of bilateral renal calculi and will have to be decided according to the merits of the particular case. Medical treatment of renal calculi has only mythical value. If a patient has passed a stone, the drinking of large quantities of distilled water, careful regulation of the diet and bowels, attention to the skin exercise, etc., may be helpful in preventing the formation of future stones. But stones once formed will never be influenced by piperazin or any other drugs and the consideration of treatment is that along surgical lines as outlined above.

CALCULOUS ANURIA

Definition and Onset.—Calculous anuria is the cessation of the urinary flow due to blockage by calculus. It may be the first symptom of the calculous disease. It comes on suddenly and is due partly to retention and partly to suppression. It occurs in a variety of ways, *viz.:* (1) When both ureters are completely obstructed simultaneously by stone; (2) by the blocking of one ureter by stone, the other kidney being absent or destroyed, either as the result of congenital abnormality (solitary kidney, or blockage of fused ureter with two kidneys), disease (pyonephrosis, etc.), or operative removal; or (3) by the blocking of the ureter of the kidney, with the development of reflex anuria in the opposite healthy kidney (doubtful occurrence).

Symptomatology.—In the beginning of a case of calculous anuria, the patient presents the same symptomatology already described under the heading of symptoms of renal calculus. It may last for a few hours or be prolonged to days. In the treatment of the condition, the side on which the pain began aids the surgeon in his line of attack. This is next followed by the tolerant stage, in which the only symptom present is suppression of urine-anuria. The latter symptom ordinarily is not absolute; in the beginning a certain amount of urine is passed, and usually a few ounces of blood-tinged urine during the twenty-four hours. Finally, complete cessation takes place. The most remarkable occurrence in this stage is the complete well-being of the patient: he not only suffers no pain, but his health both local and general are of the best. This condition persists for between five and six days. It may be prolonged for as much as sixteen days. In this stage recovery may yet occur due to relief of obstruction. This occurred in 20.8 per cent of Morris's cases. When the latter occurrence fails, and the condition is not relieved, the patient enters the uremic stage. The uremia is of the same nature and type as the uremia due to other forms of kidney disease causing destruction of its functional capacity. The uremia usually lasts about two or three days from the first symptoms of onset, which are usually hiccoughs and vomiting. From what has been said, the importance of early diagnosis and prompt remedial treatment is self-evident.

Diagnosis.—In the diagnosis of calculous anuria, the diagnostic aids available in ordinary kidney stone are often wanting. On account of anuria, ureter catheterization may prove useless and ordinary x-ray may prove impractical on account of the serious condition of the patient. When possible, however, the simple x-ray, cystoscopy, ureter catheterization, and the use of the wax tip should be employed as already outlined in discussing the diagnosis of ordinary renal calculus. When these are impractical, often sufficient data can be obtained by the physical examination of the patient. The history of preceding attacks of renal colic, tenderness in the region of the kidney on pressure, or enlargement of the kidney on palpation are important signs. The side provocative of the anuria will usually be found on the side on which the patient has colic during the premonitory stage and this is the side to attack in carrying out measures of relief.

Treatment.—The effect of expectant treatment *versus* operative treatment can be learned from the statistics of 205 cases gathered by Watson:

	Cases	*Deaths*	*Mortality*
Treated expectantly	110	80	72 per cent.
Treated operatively	95	44	46.3 per cent.
Total	205	124	

PALLIATIVE TREATMENT.—Prior to the introduction of the operative treatment, which alone offers chance of success, measures that are supportive and stimulative of renal function should be carried out, such as **hot baths and packs, salt solution** both by the **Murphy method** and **hypodermoclysis, plenty of fluids by mouth** if possible, and **pilocarpin. Massage along the region of the ureter** in the hope of dislodging the stone may be tried. **General anesthesia** of short duration may not only relieve the patient's pain if he has any, but it may also even release the stone on account of the general relaxation produced all over the body, especially in the ureter, which often is in a state of spasm.

OPERATIVE TREATMENT.—This may first be by **intravesical methods** with the catheterizing and operative cystoscope, such as removing or dislodging the stone when in the ureter. When these fail the **scalpel** may be employed. It is important to impress upon the patient and his family the gravity of the situation, even though grave symptoms are yet absent. The operation consists primarily in exposing the kidney, relieving its intense congestion, and providing an outflow of the urine by incising the kidney (nephrotomy). If the stone is within reach and easy of removal, it should be removed at the same time, but unusual protraction of the operation by looking for stone is contra-indicated. The stone can be removed later by a secondary operation, when the emergency relief has been afforded.

Pathology.—The affected kidney, either hydronephrotic or pyonephrotic, is increased to two or three times its normal size, markedly congested, has a dark purplish color and is mottled in appearance. The opposite kidney, if it is present, may show similar changes, though usually milder in degree.

CYSTS OF THE KIDNEY

Classification.—Cysts of the kidney have been classified by White and Martin, as follows: (1) Simple cysts, under which head are included small retention cysts and large serous cysts; (2) polycystic degeneration; (3) dermoid cysts; (4) paranephritic cysts; and (5) echinococcus cysts. Keyes also mentions tubercular cysts.

Multiple Small Cysts.—As the name implies, they are usually quite small, ranging in diameter, according to White and Martin, from a millimeter to a centimeter. They are usually seen in kidneys affected with chronic interstitial nephritis, and the consensus of opinion is that they are produced by the blocking up of the secretory tubules. They are located in the kidney cortex, and form projections beneath the capsule. Occasionally they occur singly. They are of no special interest except that they may possibly be confused with polycystic disease.

Large Serous Cysts.—These are also spoken of as large single cysts, solitary cysts, or hemorrhagic cysts, and are composed of several cystic cavities, containing blood or serum or both, the color of the liquid being pale or yellowish. Keyes states that the contents are never urinous. This condition is very rare, Simon having found 52 reported cases, and Brin 53. According to Herman F. Kretschmer but 48 cases have been reported since 1906. In 297 surgical diseases of the kidney, Israel found but 1 case. Albarran and Imbert have collected 31 cases, 4 of which were bilateral. Cabot's series contained 8 unilateral cysts.

ETIOLOGY.—This disease is usually found in adult life, the average age in 21 cases collected by Albarran and Imbert being forty-six years. However, it is found at both extremes, as evidenced by Rosinsky's 2 cases, one sixteen months and the other seventy-seven years of age. In Fowler's 34 cases, the extremes were four and seventy years.

It is generally conceded that it occurs more often in women than in men. According to Brin, the right kidney is more often affected than the left, and the cyst usually arises from the lower pole. There are two theories as to its origin: one, that it is a congenital malformation or the result of embryonic rests; and the other that it has the same origin as the multiple small cysts, namely, from a blocking of the uriniferous tubules in chronic interstitial nephritis. Neither theory has been proven correct.

SYMPTOMATOLOGY.—The symptoms are those of any benign growth of the kidney. When small, the patients are unaware of its existence.

When large, pressure symptoms are produced, with a sense of dragging in the kidney region. The patient may become conscious of the growth and consult a physician for this reason. Later on, digestive disturbances arise and if the tumor is very large, nutrition is interfered with, and resultant weakness and emaciation ensue. Cabot says that symptoms referable to the urinary tract are absent, as a rule, unless hematuria results from traumatism to the cyst. A case mentioned by Garceau showed definite urinary symptoms.

DIAGNOSIS.—It is difficult to make diagnosis because the signs usually are mistaken for those of hydronephrosis, ovarian cyst, or some other growth of the kidney. It is most often diagnosed at the time of exploratory operation.

TREATMENT.—Various methods of treatment have been employed such as puncture, incision and suture through the skin (marsupialization), nephrectomy, and resection. Of these, **resection** is the operation of choice unless the cyst wall is adherent to the larger renal vessels, or complications occur during the operation. Then **nephrectomy** is indicated. Some urologists prefer nephrectomy at all times, if the opposite kidney functions normally.

PATHOLOGY.—The cyst wall is thin and elastic, the color being pale or yellowish, depending upon the character of the contents. The cysts are usually of moderate size but Morris has reported one case in which the cyst contents weighed 16 pounds (6 kilograms). Cabot says that those discovered clinically are at least the size of an orange. Only a few reach a size large enough to be discovered during life. These cysts may be multiple, but when they are, one is usually much larger than the others. As a rule, the cyst is located in the cortex and according to Cabot, when arising in the parenchyma, it rarely opens into the pelvis. The wall may undergo a cartilaginous change and have various salts deposited in it. When bleeding occurs into the sac, the cyst is spoken of as hemorrhagic. The cyst wall is firmly adherent to the kidney tissue and sometimes to the surrounding viscera, making it difficult of removal.

Polycystic Degeneration—This disease is characterized by a conversion of the kidney (nearly always bilateral) into a large number of cysts, the intervening normal tissue being scant in quantity.

ETIOLOGY.—Several theories have been advanced as to its causation. Some think it is due to inflammation and plugging of the tubules with resultant cyst formation; others believe it to be due to congenital malformation, while still others believe that they are cyst adenomata. There is no convincing evidence to support any one theory, but occlusion of the tubules certainly plays an important part.

The disease may occur at any age, but most cases occur after forty and practically none between the ages of one and twenty-one years. It has been known to develop to such an extent during intra-uterine life as to interfere with labor. Cabot's collected statistics show the greatest number of cases between the ages of forty and sixty. The disease has been classified into congenital and adult types but there is no essential difference between the two.

It is slightly more prevalent in females than in males, but there is no marked difference. It is practically always bilateral, but 9 unilateral cases having been found by Seiber. However, it progresses more rapidly on one side than on the other. It has been known to occur in various members of the same family, but heredity is not an important causative factor.

Associated Lesions.—This condition is frequently associated in adults with cyst formation in the liver. Cardiac hypertrophy and arteriosclerosis are frequent concomitants. In the congenital form all sorts of malformations have been found associated, such as cleft palate, imperforate anus, cysts of the ovary, supernumerary digits, talipes, etc.

Symptomatology.—The disease runs a course, with symptoms similar to those of chronic interstitial nephritis, unless the tumor becomes noticeable because of its size. There is local pain and tenderness, at first unilateral, later bilateral. The dull aching pain is due to distention of the renal capsule, while the paroxysmal attacks of colic are due to the passage of clots. Hematuria may occur. Later on, symptoms of kidney insufficiency develop and finally uremia. The changes in the urine are those of interstitial nephritis. Tumor, pain, and hematuria are the surgical symptoms present.

Diagnosis.—This is very difficult because it is an insidious growth, and resembles so closely in symptoms chronic interstitial nephritis. Statistics show, that very few are diagnosed during life. If, however, bilateral knotty renal tumors are discovered, with the signs and symptoms of chronic interstitial nephritis or uremia, the true nature should be suspected. Renal functional tests are of great value, especially relative renal excretory functional tests. If the tumor is unilateral, it is very hard to diagnose, as malignancy is at once suspected. Pyelography will help to distinguish the condition from solid tumors and in determining the true condition. The author has been able to diagnose before operation 2 cases seen by him. It is also to be differentiated in diagnosis from the various other kidney cysts and pyo- and hydronephrosis.

Treatment.—The treatment is that of chronic interstitial nephritis, unless conditions are favorable to operation or symptoms and complications call for special treatment. Pelvic lavage may control bleeding. Nephropexy may be beneficial, if the size of the growth has caused the kidney to become movable with resultant kinking of the ureters. Decortication has been tried to prevent alarming uremic symptoms but is ineffective. **Rovsing's operation** or **puncture of the larger cysts** is said by most authorities to be the operation of choice, as it relieves compression and helps to prevent the formation of new cysts by relieving obstruction. Partial nephrectomy may be tried if the growth is limited to one portion of the kidney, but the cause of its limited application and frequent failure is evident. **Total nephrectomy** is indicated if there is uncontrollable hemorrhage, or if the function of one kidney is practically or entirely destroyed, the other kidney being fairly normal. The bilateral nature of the disease limits its scope and the mortality is high.

Prognosis.—This depends upon the rate of cyst formation and the relative involvement of each kidney. If unilateral, the patient may live for years. The age of onset also plays an important part, intra-uterine cases resulting in death soon after birth and infantile patients living only a short time. Death is usually due to uremia or some terminal infection.

Duration.—According to Morris, adults survive from one to ten years. One patient lived twenty-two years after diagnosis. Boinet and Rebaud state that 50 per cent. of children congenitally affected die immediately after birth.

PATHOLOGY.—Grossly one sees a large number of cysts scattered throughout the kidney and just beneath the capsule, causing the surface to appear very irregular which latter characteristic is said by Keyes to be so striking that it is all but pathognomonic of the disease. With the exception of the knobby appearance of the surface, the general contour of the kidney is more or less preserved. Occasionally one cyst is so much larger than the others that this is not true. The tumor may reach enormous proportions as evidenced by Morris's case, in which the tumor weighed 16 pounds (6 kilograms). In the average case, however, the kidney is several times its normal size. The color varies, depending in a large measure upon the nature of the cyst contents. The latter may be liquid, viscid, serous, or colloid. Cabot says that the cystic contents may be urinous, but Keyes denies this. The larger cysts may be dark and hemorrhagic. The walls of the cysts are separated by abnormal kidney parenchyma or fibrous tissue. Microscopically, the cyst wall is lined with flattened epithelium, which in places has proliferated, causing projections into the cyst cavity. The tubules and malpighian capsules are seen in various stages of cyst formation.

Dermoid Cysts.—These are extremely rare, and differ in no respect from similar cysts in other parts of the body. The cyst is composed of hair and a material containing epithelium and products of degeneration. The diagnosis can be made only by the passage of hair in the urine or by section of the cyst. Nephrectomy gives the only relief.

Paranephritic Cysts.—These are usually the result of perinephritic hematomata which have become encapsulated. They may be hydatid in nature, or according to White and Martin, they may be the result of embryonic rests. They may arise from the capsule of the suprarenal gland. They are unilateral and single and produce symptoms only because of their size. Malignant changes may occur, particularly sarcomatous. Excision of smaller growths is easy but considerable difficulty may be encountered with the larger ones.

Echinococcus Cysts.—ETIOLOGY.—Hydatid cyst is the cystic stage in the life cycle of a cestode, known as the tinea echinococcus. This condition is not often encountered in this country; it is not uncommon in Europe, but quite common in Australia and the Argentine Republic and is extremely prevalent in Iceland. In the latter country 16 per cent. of the population is supposed to be infected. The eggs are ingested with food and water, hatch into embryos in the stomach and intestines, and by means of hooklets burrow into the walls of the stomach or gut, whence they enter the venous system. This explains the apparent predilection of the disease for the lungs and liver, as the blood reaches these organs before it passes on to the kidney. Edward L. Young, Jr. states that the relative proportion of kidney cases to all others is as 1 is to 5, while White and Martin state that from 5 to 8 per cent. of all cases occur in the kidney. The condition may be found at any age, but most cases occur in adult life. It shows no preference for either sex and is usually unilateral, the left kidney being nearly always the one affected. The disease begins in the cortex just beneath the capsule, but any portion of the kidney may be later involved. It has been known to have its origin in the perirenal tissue. The cyst wall is composed of two layers, an outer or hydatid, and an inner or germinal. In the fluid contents are found the hooklets. Around the cyst wall is dense fibrous tissue formation with no definite line of demarcation. The cyst grows slowly, as a rule, and the kidney tissue undergoes compensatory hypertrophy so that the condition may exist for years without alarming symptoms. Trauma may produce suppuration in the cyst and general pyemia may follow.

SYMPTOMATOLOGY.—When small, there may be no symptoms. When of large size, unless the cyst ruptures, the symptoms are those produced by weight and pressure, namely, a sense of aching and dragging in the kidney region. Acute pain is not often present. Pressure on the surrounding organs, such as stomach or gut, may cause only mild digestive disturbances, but occasionally symptoms of intestinal obstruction. Rupture into the surrounding viscera causes pyonephrosis with its resultant symptoms, and rupture into the kidney pelvis causes renal colic and nearly always hematuria. The ureters may become blocked, causing hydronephrosis. Rupture into the peritoneum causes mild peritonitis, as a rule, and urticaria or severe anaphylactic reaction. Occasionally the tumor is discovered accidentally by the patient.

DIAGNOSIS.—Bismuth x-rays will differentiate this condition from other abdominal tumors and radiographs of the kidney will show its connection with that organ. It is ordinarily mistaken for hydronephrosis or ovarian cyst but hypernephroma and polycystic kidney may be confused with it. A fixation test, described by Lamboy and Parver, is supposed to be specific. The use of the x-ray and the measuring of the capacity of the renal pelvis will rule out hydronephrosis. Hydatid thrill is rarely obtained. After rupture into the pelvis a positive diagnosis can be made by finding the hooklets in the urine. Eosinphilia is usually present.

TREATMENT.—As soon as the disease is diagnosed, **operation** should be advised, its nature depending upon conditions encountered. If the process is limited, with no complications, resection may be the operation of choice. White and Martin recommend **aspiration** of the cyst, followed by injection of a 5 per cent. **formaldehyd solution**, and a few minutes later **dissection of the cyst wall** and **closure of the remaining cavity by suture.** If suppuration is present, they recommend **drainage.** Edward L. Young, Jr. prefers **marsupialization** in all of the very large cysts and some of the smaller ones, stating that it is simplest and safest and in the end gives good results. If the kidney substance is extensively involved or destroyed, **nephrectomy** is the operation of choice.

Prognosis.—The disease may be harmless or terminate fatally. Occasionally, spontaneous recovery follows rupture into the pelvis or the cyst may die. This, however, is rare. Rupture into the surrounding organs or peritoneum is a serious complication.

Tubercular Cysts.—These occur during the course of kidney tuberculosis, and are dealt with in the chapter on kidney tuberculosis.

RENAL TUMORS

Introductory.—Primary tumors of the kidney, although somewhat rare as compared to tumors originating in other organs and tissues of the body, are none the less important and of great clinical interest. Metastatic tumor growths in the kidney are quite common but ordinarily are not recognized until the primary growth is well advanced. It has been estimated that from 0.8 to 1 per cent. of malignant tumors originate in the kidneys and a much smaller percentage of benign tumors occur in this organ. Malignant renal growths are unique in that a fairly large proportion occur in children. Considerable controversy as to the exact pathological nature and origin in the embyronic structures of some of these tumors is still in progress. Although such exact knowledge of the origin of these malignant tumors is of great pathological interest, it is not so essential to the general practitioner and surgeon whose chief objects are early recognition and effective treatment. That classifications of renal neoplasms are unsatisfactory is evidenced by the great number and variety of classifications. The following is a list of renal growths divided into two groups according to their clinical behavior:

Benign Growths

- Adenoma
- Fibroma
- Lipoma
- Angioma
- Papilloma

Malignant Growths

- Hypernephroma
- Carcinoma
  - Adenocarcinoma
  - Papillary Carcinoma or Papillary Epithelioma
  - Squamous-cell Carcinoma or Epithelioma (Nonpapillary)
- Sarcoma
  - Round Cell
  - Spindle Cell
- Embryonic Tumors
  - Teratoma
  - Rhabdomyoma
  - Mixed Tumors

Benign Renal Tumors

Classification.—The most important feature of benign kidney growths is their strong tendency to undergo malignant changes. With the exception of benign growths situated in the kidney pelvis they do not give rise to any symptoms and hence are recognized only accidentally during operation or at autopsy.

Adenomata.—They are quite rare in the kidney. They appear as grayish-red nodules in the cortex; sometimes they attain large size, but usually remain small. Microscopically they are seen to be composed of ramifying tubular or glandular structures lined with epithelial cells similar to those of the convoluted tubules.

Fibromata.—These are usually small and appear as firm, round, grayish nodules displacing renal tissue in the cortex or pyramids. Microscopic examination shows an atypical fibrous tissue and often an admixture of smooth muscle.

Lipomata.—These are rare in the kidney. They are usually quite small and situated under the capsule. In addition to the fat these tumors often show smooth muscle and other elements.

Angiomata.—These are very rare in the kidney. They are usually situated below the capsule and remain quite small. Occasionally they may originate in the renal pelvis. The most generally accepted theory as to their origin is that of Ribbert, namely, that they grow independently from a rudiment which is destined to form blood-vessels.

Papillomata.—Although they are in the beginning certainly benign and usually classed as such, they show a strong tendency to become malignant and are then papillary carcinomata. They are the commonest tumors of the renal pelvis, and may be single or multiple. Usually they are unilateral, but they may be bilateral. These tumors originate in either the mucosa of the kidney pelvis or in that of the ureter. Papillomata originating in the kidney pelvis often spread to the ureter. or *vice versa.* Like papillomata of the bladder these tumors tend to recur after removal and finally become carcinomata. Grossly, papillomata appear as branching soft tufts composed of numerous delicate villi closely packed together. Microscopically, the villi are seen to have a central blood-vessel which is surrounded by the typical stratified epithelium of the renal pelvis. The cells are held together by loose connective tissue.

Symptomatology.—When situated within the renal parenchyma, benign tumors, unless they attain large size, are symptomless, and therefore are of no importance surgically. When of large size, the tumor will produce pressure symptoms,—pain, edema, varicocele, and gastrointestinal disturbance. However, when located in the kidney pelvis, these tumors frequently give rise to symptoms. Angiomata may rupture and result in serious hemorrhage.

Papillomata bleed intermittently but ordinarily the hemorrhage is not large. Pain may or may not accompany hematuria, but when large clots are passed, colicky pain occurs. The growth together with a clot may fill the entire pelvis and obstruct the ureter, giving rise to a hematonephrosis. A tumor may then be palpated and the patient will have pain due to pressure.

Diagnosis.—Inasmuch as the symptoms when present at all are the same for the most part with benign as with malignant tumors of the kidney, it is practically impossible to distinguish between them before operation. Slow growth and less marked symptoms are features which may give one the impression that a given tumor is benign. Of course in the late stages of malignancy with metastases and cachexia, the diagnosis is quite evident, but it is also too late to be of much benefit to the patient. Benign tumors producing symptoms are dealt with in the same manner as malignant tumors so that from the standpoint of treatment it is not a matter of great importance to distinguish them before operation. The same diagnostic methods apply in the diagnosis as will be mentioned under malignant tumors.

Treatment.—The diagnosis of renal tumor demands **nephrectomy.** This procedure is warranted with tumors which apparently are benign, not only to completely relieve symptoms, but also because of the very strong tendency to malignant transformation.

MALIGNANT RENAL TUMORS

Classification.—The so-called hypernephromata are by far the most important and the most frequent tumors of the kidneys. In adults these growths greatly outnumber any other; in children the embryomata compose the larger proportion. An idea of the relative frequency of the different types of malignant growths may be obtained from the following reports. Garceau in a study of the surgical and autopsy material for ten years at the Massachusetts General Hospital and Boston City Hospital reports the following:

Perirenal sarcoma	1
Papilloma of renal pelvis	1
Hypernephromata of renal parenchyma (large)	33
Hypernephromata of renal parenchyma (small)	12
Carcinomata of renal parenchyma	3
Papillary cystadenomata of kidney parenchyma	4
Papillary adenomata of kidney parenchyma	11
Sarcoma of kidney parenchyma (round cell)	1
Sarcoma of kidney parenchyma (spindle cell)	1
Fibromata	14
Lipomata	5
Total	86

Hypernephromata thus make up 52.33 per cent. of all renal growths in this list. Excluding the tumors which are definitely benign, hypernephromata compose 68.17 per cent. of the malignant growths.

Louis B. Wilson in a study of 92 tumors at St. Mary's Hospital, Rochester, Minn., reports the following:

Hypernephromata or mesotheliomata	71
Embryomata	3
Wolffian tumor	1

Sarcomata	7
Adenoma	1
Fibroma	1
Papillomata of renal pelvis	3
Carcinomata of renal pelvis	4
Squamous-celled epithelioma	1
Total	92

In this list hypernephromata make up 77.17 per cent. of all tumors. Owing to the difference of opinion among various authors as to the criteria of classifying these tumors there are diversities in different tables. For this reason many reports, especially the older ones, are of little value in studying the frequency of the types. The above figures perhaps give one a correct impression of the proportion of each variety of renal growths as they are at present classified.

HYPERNEPHROMATA.—The term hypernephromata is applied to a group of tumors which according to Grawitz originate in small misplaced masses of adrenal tissue (adrenal rests) which are so frequently found imbedded in the substance of the kidney. Before Grawitz directed attention to these tumors they were variously grouped as lipomata, sarcomata, or carcinomata. The theory of origin from adrenal rests has received very general approval, but from time to time numerous other theories have been advanced. A theory which recently has been gaining favor is that presented by Louis B. Wilson, who contends that these tumors develop from islands of nephrogenic tissue which have failed to connect with the renal pelvis. He accordingly applies the term "mesotheliomata" to these tumors.

Grawitz presented the following five reasons for his conclusion: (1) The position of these tumors underneath the capsule where adrenal rests are often found normally; (2) cells are singular in type to adrenal cells; (3) characteristic fatty infiltration of the cells which is never found in the kidney epithelium; (4) the presence of a limiting capsule; and (5) the arrangement of the cells in relation to the stroma similar to that of adrenal cortex.

The following reasons as stated by Stoerck are presented to disprove the theory of Grawitz: (1) The Grawitzian tumors most frequently develop at the lower pole of kidney, where adrenal rests are not found; (2) the so-called fat of the cells of the Grawitzian tumors is usually not fat, but a vacuolation related to the glycogen content of the cells; (3) the Grawitzian tumor is a tumor of the renal cortex and not of the renal capsule in which the adrenal rests are usually found; and (4) the Grawitzian tumors almost invariably contain tubules the analogues of which are never seen either in the normal suprarenal or in tumors of that gland.

Stoerck suggested that these neoplasms arise from regenerating convoluting tubules in the atrophic kidney.

Glynn adds the following reasons to disprove the adrenal origin of these tumors: (1) Histologic dissimiliarity between tumors of the kidney and adrenal gland; (2) renal tumors never influence growth of sexual characteristics; and (3) why should adrenal rests, though comparatively rare in the kidney, produce hypernephroma, the commonest renal tumor, while adrenal rests in other localities though comparatively common so rarely produce tumors either benign or malignant?

At present it may be stated that hypernephromata comprise a group of tumors which are peculiarly different in their histological characters from other tumors and stand out in a separate group. Their exact origin is still unsettled. Clinically, however, these tumors are well understood.

Hypernephromata vary in size and may be situated in any other part of the kidney. The larger growths compress and distort the normal renal tissue. They appear usually as soft, yellowish nodules which may vary from a very minute size to the size of an adult head. Less frequently they are brownish or grayish due to secondary changes. Ordinarily they are encapsulated, but in the later stages of development the capsule may rupture, and the growth spread into contiguous structures.

A cut section shows a glistening yellow surface and in the larger tumors grayish areas of necrosis and cystic cavities filled with blood. Microscopically the tumor is seen to consist essentially of large polygonal or cubical pale transparent cells and small nuclei, resembling closely the cells of the adrenal cortex. The cells are held together by a fine stroma in which there are numerous thin-walled blood-vessels. A striking feature is the situation of cells directly upon the capillary walls. Usually the cells have an alveolar arrangement; less frequently a papillary formation is observed.

These growths metastasize almost exclusively through the blood stream. Frequently specimens are observed with the growth extending directly into the renal vein. Metastases may be disseminated in all parts of the body. The most frequent locations of metastases, however, are the lungs and long bones. Although some hypernephromata remain small and never metastasize, as shown by the incidental discovery of such growths at autopsy, it is nevertheless desirable to consider the entire group malignant.

Carcinomata.—These are distinctly tumors of adult life, being rare before the fourth decade. According to the present standards of classification true carcinomata compose only a small percentage of renal tumors. Formerly many growths now designated as hypernephromata were placed in this group. Carcinomata of the parenchyma have their origin in the tubular epithelium. Metastasis occurs through both the blood and lymphatic circulations.

Due largely to early metastasis the primary growth seldom attains large size and the kidney is not much distorted. There are often areas of necrosis, hemorrhage or cyst formation. Grossly these tumors have no very characteristic appearance. Microscopically they are seen to consist of rather large irregularly shaped epithelial cells with granular cytoplasm and large nuclei containing several nucleoli. The cells are held together by a connective tissue stroma. In many specimens the cells are found in irregular groups without any definite arrangement. In other specimens the cells are arranged in strands.

ADENOCARCINOMATA.—These tumors represent the malignant stage of adenomata and by many are termed "malignant adenomata." They often are of large size. Some of the alveolar spaces are filled with cystic fluid. Within such cysts the epithelium may be thrown up in papillary folds, and the growth may be termed papillo-adenocarcinoma, or papillary adenocystoma.

PAPILLARY CARCINOMATA (PAPILLARY EPITHELIOMATA).—These tumors occur in the renal pelvis and represent the malignant stage of the simple papillomata. They seldom attain very large size on account of the early accompanying profuse hemorrhage.

SQUAMOUS-CELL CARCINOMATA (NONPAPILLARY EPITHELIOMATA).—These originate in the mucosa of the renal pelvis or ureter. They cause hematonephrosis and give rise to hematuria.

SARCOMATA.—These are chiefly of the round-cell or spindle-cell variety. Although not so rare, they are not so common as other varieties of malignant growths. In Garceau's collection of 86 renal growths, there are 2 sarcomata, round-cell and spindle-cell. They originate chiefly in the fibrous tissue of the renal cortex. Usually they are comparatively small, uneven, soft grayish masses. Metastases occur through the blood stream.

TERATOMATA, RHABDOMYOMATA AND MIXED TUMORS.—These are closely related and are often grouped as embryonic tumors. They are distinctly tumors of childhood. Binney in a collected series of 114 cases of renal growths reports 27 embryomata. Their origin is still a subject of controversy. The general opinion, however, is that they originate in an isolation of a blastomere in the developing embryo, resulting in a displacement of tissue normally found in other regions of the body. Such growths often attain very large size, weighing as much as 6 pounds (2.2 kilograms). The gross appearance is quite variable.

Teratomata contain tissues representing all three germinal layers. Thus skin and its appendages, teeth, convoluted structures resembling intestine, cartilage and thyroid tissue may be found. Although teratomata are benign, it is not at all uncommon for carcinoma to develop at some point in their epithelium (MacCallum). Dermoid is a simple form of embryonic growth composed chiefly of epithelial structures.

Rhabdomyomata are composed essentially of muscle fibers but usually also have an admixture of other supporting tissue elements as cartilage and connecting tissue, and sometimes epithelium. Mixed tumors are composed of an agglomeration of various kinds of cells: Epithelial cells in glandular formation, about which are striated and unstriated muscle fibers, connective tissue, cartilage and often sarcoma tissue. They grow rapidly and metastasize through the blood stream.

COMBINED TUMORS.—In the same kidney two or more growths of entirely different types may be found. Graves and Templeton recently reported two such cases and reviewed the literature. One case showed papillary carcinoma in the pelvis and hypernephroma. The other case showed papilloma of renal pelvis and papillary cystadenoma of kidney.

Etiology.—Age.—The extremes of age, under five years and over forty years are the periods of renal malignancy. This is well shown in Koster's table as shown by Keyes:

From birth to 5 years	128 cases
Six to ten years	41 cases
Forty to fifty years	125 cases
Over fifty years	128 cases
Total	422 cases

Sex.—Most writers state that males are affected more often than females. No explanation for this difference, however, is stated. Of 74 cases reported by Barney, 43 were in males and 31 in females. In a study of 83 cases, Braasch found 62 per cent. in males.

Heredity and trauma are not causative factors. Trauma, however, may excite hemorrhage in a tumor that was previously symptomless. Chronic infections and calculi in the renal pelvis are the effects rather than causative factors in renal tumors. Both kidneys are about equally affected.

Symptomatology.—Hematuria, pain and tumor are the three classical symptoms of renal tumor. Only one symptom may be present for a long period. When all are present, the new growth is well advanced and perhaps so far as to preclude the possibility of cure. Hinman found all three of these symptoms present in an average of 38 per cent. of cases at the time the patients presented themselves for treatment. In a study of 83 cases Braasch found as the first symptom hematuria in 47 per cent., pain in 32 per cent. and tumor in 15 per cent.

Hematuria is the most important single symptom. Ordinarily, in the beginning at least, hemorrhage is not large and may be just sufficient to tinge the urine. In some cases, however, hemorrhage is large and clots may fill the pelvis and ureter giving rise to renal colic. The blood appears spontaneously, lasts several days and may not be noticed again by the patient for months or even years. Unfortunately this complete spontaneous disappearance of the symptoms often serves to reassure the patient and proper investigation is deferred. Hematuria always demands a most thorough examination of the urinary tract. In children hematuria is not very frequent.

Pain is quite variable in character, location, intensity and duration. The growth itself or an obstruction of the ureter with filling of the pelvis may press upon nerves and nerve-endings, resulting in pain often of the dull aching character. The pain may be situated in the loin on the affected side or be referred to abdomen or opposite side. Pain due to passage of a clot through the ureter is of the colicky variety and is referred to the affected kidney region and groin.

Renal tumors in children usually are not recognized until a palpable mass makes its appearance. The tumors which are chiefly of the embryonal type grow rapidly and attain large size, making them readily palpable in the hypochondrium. In adults a tumor is not palpable until the new growth is well advanced. Even when of fairly large size a renal tumor is *not often* palpable, especially in persons with thick abdominal *walls*. A mass due to renal tumor appears in the upper abdomen just to one side of the midline. The tumors vary in size and consistency. They may feel hard and nodular or soft and smooth. Before the growth has extended outside the kidney the tumor is movable; after extension into adjacent structures the mass is firmly fixed and usually the condition is then inoperable. A renal mass due to pelvic new growth with hematonephrosis may be intermittently palpable, as pointed out by Israel. When not palpable by bimanual palpation in the prone position, renal tumors can sometimes be felt with the patient in the lateral position.

URINARY FINDINGS.—During active hemorrhage blood is readily recognized in the urine. Microscopic blood may be found when no other symptoms are present. In some cases pus cells are found, due to an accompanying inflammatory process. Barney has recently reported a case in which inflammatory symptoms (fever, leukocytosis and pyuria) entirely overshadowed the symptoms of tumor.

PRESSURE SYMPTOMS.—Due to compression of the spermatic vein, particularly when the tumor is on the left side, varicocele of large size may appear. Pressure upon the large veins within the abdomen in the late stages causes ascites and edema of the lower extremities. A right-sided tumor or extension to the liver may result in jaundice. Severe neuralgia may be caused by pressure upon nerves. Intestinal obstruction may be caused by a large tumor.

Gastro-intestinal disturbances as anorexia, indigestion, constipation or diarrhea are sometimes prominent symptoms. Fever, usually of moderate degree, is present in a small percentage of cases. In the late stages anemia and cachexia develop.

Diagnosis.—The diagnosis must be made early if one is to hope for cure of these cases. It is well recognized that early diagnosis is quite difficult and at times impossible, due to lack of symptoms or to the vague indefinite nature of the symptoms. Often the symptoms are mild for a time and disappear spontaneously so that the patient and sometimes the physician feels assured that no serious trouble exists. At present, however, we possess certain exact methods of investigating the urinary tract and it is only by utilizing these methods in cases that present the slightest suspicion of renal tumors that we can make early diagnosis. The typical late cases presenting all the classical symptoms, hematuria, pain of the characteristic type and tumor, are readily recognized.

Cases presenting one or more of the symptoms suggesting renal tumor should be investigated by urinalysis, cystoscopy and catheterization of ureters, pyelography, and radiography.

In complete urinalysis, careful urine examination may show red blood-cells, pus cells and albumin.

In cystoscopy and catheterization of ureters, more information will be obtained if cystoscopic examination is made during the period of hematuria. The ureter opening on the affected side may be congested and irregular in appearance. Blood may be seen issuing from the ureter opening or a blood-clot may be protruding from the ureter. Blood in specimens obtained by ureteral catheters may be entirely of traumatic origin, due to introduction of catheters and has no diagnostic value.

Catheters should be introduced into both ureters and the functional capacity of each kidney determined by phenolsulphonephthalein or other methods. There may be marked impairment or no function on the affected side due to destruction of renal tissue or obstruction of the pelvis and ureter with a clot. In early cases there may be no impairment of function on the affected side.

Pyelography is of paramount importance in the diagnosis of renal tumor. By this procedure the characteristic changes in the renal pelvis can be observed. The chief deformities noted are retraction of one or more calyces producing the so-called "spider leg" deformity, irregular pelvic dilatation, dilatation of the upper ureter, or the position of the pelvis may be changed.

Radiography may show the outline of the mass, and the presence or absence of calculi.

The diagnosis as to the type of malignant renal growth is quite impossible before operation. The following conditions are to be differentiated from renal new-growth by the proper methods: Renal calculus, renal tuberculosis, essential hematuria, hydronephrosis, floating kidney, tumor of spleen, tumor of liver, tumor of pancreas, tumor of intestine and tumor of ovary.

Treatment.—Early nephrectomy is the only treatment. This procedure is to be advised if the unaffected kidney is sufficient to maintain life, providing the tumor is removable and providing there are no metastases. Operation, however, is sometimes performed to relieve pain in cases beyond hope of cure. After nephrectomy **radium** and **x-ray therapy** may be employed in the hope of preventing recurrence.

Course and Prognosis.—Renal malignancy without operation is inevitably fatal. The course especially of hypernephromata is often slow. In Garceau's cases the average duration of symptoms of hypernephromata was two years and three months.

Carcinomata and sarcomata may run a much more rapid course. After careful removal of the tumor by operation one can never be certain that the growth will not recur.

BIBLIOGRAPHY

Pyelitis

CABOT, H., AND CRABTREE, E. G. A classification of renal infection with particular reference to treatment. Bos. Med. & Surg. Jour., 1916, clxxiv, 780.

——— Colon bacillus pyelonephritis: Its nature and possible prevention. Trans. Section. Gen.-Urin. Diseases, A. M. A., 1916, lxvii, 209.

CASPER, L. Genito-Urinary Diseases, 1906, P. Blakiston's Son & Co., Philadelphia.

Chetwood, C. H. Practice of urology, 1921, p. 603, W. Wood & Co., New York.
Crabtree, E. G. Observations on the etiology of renal infection. Lancet-Clinic, 1916, cvi, 99.
Eisendrath, D. N., and Kohn, J. V. Rôle of lymphatics in ascending renal infection of the urinary tract. Trans. Section Gen.-Urin. Diseases, A. M. A., 1916, lxvi, 561.
Geraghty, J. T. The treatment of chronic pyelitis. Trans. Section Gen.-Urin. Diseases, A. M. A., 1914, p. 113.
Kelly, H. A., and Burnam, C. F. Diseases of the kidneys, ureters and bladder, Vol. II, p. 219, 1914, D. Appleton & Co., New York.
Keyes, E. J., Jr. Diseases of genito-urinary organs, p. 367, 1912, D. Appleton & Co., New York.
Koll, I. S. The experimental effect of the colon bacillus on the kidney. Trans. Section Gen.-Urin. Diseases, A. M. A., 1914, p. 104.
Kretschmer, H. L. The treatment of pyelitis. Surg., Gyn. & Obstet., 1921, xxxiii, 632.
Kretschmer, H. L., and Helmholz, H. F. The treatment of pyelitis in infancy and childhood. Jour. Amer. Med. Assoc., 1920, lxxv, 1303-5.
Osler, Sir Wm. Practice of medicine, p. 681, D. Appleton & Co., New York.
Quinby, W. C. Pyelitis in children. Trans. Gen.-Urin. Section, A. M. A., 1916, lxvii, 218.
Watson, P. S., and Cunningham, J. H. Genito-urinary diseases, 1908, Lea & Febiger, Philadelphia.
White and Martin. Genito-urinary and venereal diseases, p. 626, 1920, J. B. Lippincott Co., Philadelphia, Pa.

Hydronephrosis

Braasch, W. F. Perinephritic abscesses. Surg., Gyn. & Obstet., 1915, xxi, 631.
Cabot, H. Urology, Vol. II, p. 432, 1918, Lea & Febiger, Philadelphia, Pa.
Cabot, H., and Crabtree, E. G. Frequency of recurrence of stone in kidney after operation. Surg., Gyn. & Obstet., 1915, xxi, 223.
——— Colon bacillus pyelonephritis: Its nature and possible prevention. Trans. Section Gen.-Urin. Diseases, A. M. A., 1916, lxvii, 209.
Casper, L. Genito-urinary diseases, 1906, P. Blakiston's Son & Co., Philadelphia, Pa.
Caulk, J. R. Ureter catheter drainage in the treatment of renal infections with special reference to the infected hydronephrosis complicating pregnancy. Jour. Amer. Med. Assoc., 1917, lxviii, 675.
Chetwood, C. H. Practice of urology, 1921, Wm. Wood & Co., New York.
Crabtree, E. G. Some operations on the etiology of renal infections. Lancet-Clinic, 1916, cvi, 99.
Geraghty, J. T. The treatment of chronic pyelitis. Jour. Amer. Med. Assoc., 1914, lxiii, 2211.
Hinman, F. Urinary antisepsis: A clinical and bacteriologic study. Jour. Amer. Med. Assoc., 1915, lxv, 1769.
Keyes, E. L., Jr. Diseases of the genito-urinary organs, p. 505, 1910, D. Appleton & Co., New York.
Koll, I. S. The experimental effect of the colon bacillus on the kidney. Trans. Gen.-Urin. Section, A. M. A., 1914, lxii, 104.
Kretschmer, H. L. Pyelitis follicularis. Surg., Gyn. & Obstet., 1913, xvii, 612.
Kretschmer, H. L., and Helmholz, H. F. The treatment of pyelitis in infancy and childhood. Jour. Amer. Med. Assoc., lxxv, 1920, 1303.
Quinby, W. C. Pyelitis in children. Trans. Gen.-Urin. Section, A. M. A., 1916, lxvii, 218.
Watson, P. S., and Cunningham, J. H. Genito-urinary diseases, 1908, Vol. II, p. 1129, Lea & Febiger, Philadelphia, Pa.

White and Martin. Genito-urinary surgery and venereal diseases, 1920, p. 505, D. Appleton & Co., New York.

Cysts of the Kidneys

Cabot, H. Modern urology, 1918, p. 650, Lea & Febiger, Philadelphia, Pa.

Chetwood, C. H. Practice of urology, 1921, p. 554, Wm. Wood & Co., New York.

Keyes, E. L., Jr. Genito-urinary diseases, 1905, p. 545, D. Appleton & Co., New York.

Kelly and Burnam. Diseases of the kidneys, ureter, and bladder, 1914, Vol. II, p. 367, D. Appleton & Co., New York.

White and Martin. Genito-urinary and venereal diseases, 1905.

Young, E. L., Jr. The chemical and pathological evidences of the possibilities of spontaneous healing of renal tuberculosis without total destruction of the kidney. Jour. Amer. Urol. Assoc., Brookline, 1916.

Renal Tumors

Barney, J. D. Malignant diseases of the kidney with unusual symptoms. Bos. Med. & Surg. Jour., 1920, clxxxiii, 710.

——— The symptomatology of renal tumors: A study of 74 cases from Massachusetts General Hospital, Boston Med. and Surg. Jour., clxviii, 1913, 300.

Berg, A. A. Malignant hypernephroma of the kidney: Its clinical course and diagnosis with a description of the radical operative 'cure. Surg., Gyn. & Obstet., 1913, xvii, 463.

Binney, H. Cabot's Modern urology, 1918, Vol. III, p. 603, Lea & Febiger, Philadelphia, Pa.

Braasch, W. F. Clinical data on malignant renal tumors. Jour. Amer. Med. Assoc., 1913, lx, 274.

Colson, J. A. C. Value of pyelography in the diagnosis of neoplasms of kidney. Jour. Urol., 1921, v, 67.

Garceau, E. Renal, ureteral, perirenal and adrenal tumors, 1909, D. Appleton & Co., New York.

Glynn, E. E. The adrenal cortex, its rests and tumors: Its relation to other ductless glands, and especially to sex. Quart. Jour. Med., Oxford, 1911-12, v, 157.

Graves, R. C., and Templeton, E. R. Combined tumors of the kidney. Jour. Urol., Balto., 1921, v, 517.

Grawitz, P. Die sogenannten Lipome der Niere. Virchow Arch., 1883, xciii, 39.

Hyman, A. Tumors of the kidney. Surg., Gyn. & Obstet., 1921, xxxii, 216.

Hinman, F. Early diagnosis of renal tumor with the report of five cases and the demonstration of several pyelograms illustrative of the difficulty. Surg., Gyn. & Obstet., 1917, xxiv, 669-680.

Keyes, E. L., Jr. Textbook of urology, 1920, D. Appleton & Co., New York.

Lawrie, T. F. Tumors of the kidney: Report of three cases. New York State Med. Jour., 1921, xxi, 279.

Mac Callum, W. G. Textbook of pathology, 1918, W. B. Saunders Co., Philadelphia, Pa.

McGown, P. E. Papillomatous epithelioma of kidney pelvis. Jour. Amer. Med. Assoc., 1920, lxxv, 1191.

Miller, E. M., and Herbst, R. H. Papillary epithelioma of kidney pelvis. Jour. Amer. Med. Assoc., 1921, lxxvi, 918.

Perrin, E., and Aigrot, G. Epithelioma in kidney pelvis. Jour. Amer. Med. Assoc., 1921, lxxvi, 275.

Porter, L., and Carter, W. E. Observations on tumors of kidney region in children. Trans. Sec. Dis. Children. A. M. A., 1920, lxxvi, 181.

Ribbert, H. Über Bau. Wachsthum und Genese der Angiome, nebst Bemerkungen über Cystenbildung. Virch. Arch., 1898, cli, 381.

Roland, S. Papillary tumor in renal pelvis. Jour. Amer. Med. Assoc., 1920, lxxv, 1752.

Stevens, W. E. Tumors of the renal pelvis. Jour. Amer. Med. Assoc., 1920, lxxiv, 1576.

Stoerck, H. Zur Histogenese der Grawitzischen Nierengeschwiilste. Beitr. z. path. Anat. u. z. allg. Path., Jena, 1908, xliii, 393.

Wilson, L. B. The embryogenetic relationship of tumors of the kidney, suprarenal and testicle. Ann. Surg., 1913, lvii, 522-534.

SECTION IX

DISEASES OF THE BLOOD

CHAPTER I

INTRODUCTION AND CLINICAL METHODS OF BLOOD EXAMINATION

BY CHARLES LYMAN GREENE, M.D.

Definition, p. 740—Functions of the blood, p. 740—Importance in diagnosis, p. 740—Morphologic vs. chemical and physical examinations, p. 741—Commonly used terms, p. 741.

Erythrocytes, p. 742—The red blood-cells, p. 742; Abnormal forms, p. 743; Evidences of regeneration, p. 743; Unusual erythrocytic staining reactions, p. 743; The normoblast, p. 744; The megaloblast, p. 744; The microblast, p. 744; Mesoblasts, p. 744; Basophilic erythrocytes, p. 744; Maurer's spots, p. 744; Schüffner's stippling, (Schüffner's spots), p. 745; Howell's bodies, p. 745.

The leukocytes, p. 745—Normal leukocytic forms, p. 745:—The polymorphonuclear neutrophil, p. 745; The small lymphocyte, p. 745; The large mononuclear leukocyte, p. 745; The transitional leukocyte, p. 745; Eosinophils, p. 745; Basophils, p. 745—Unusual or abnormal forms, p. 746:—Significance, p. 746; The metamyelocyte, p. 746; The myeloblast, p. 746; Promyelocytes, p. 746; Türck's irritation forms, p. 746; Giant marrow cells, p. 747; Lymphoblasts, p. 747; Giant lymphocytes (pathologic lymphoblasts), p. 747; Melanemia, p. 747; Idiophilia, p. 747; Perinuclear basophilia, p. 747; The inclusion bodies of Döhle, p. 747; Plasma-cells, p. 748.

Essential laboratory procedures, p. 748—The coloring matter of blood, p. 748—Technic of blood examination, p. 748:—To obtain blood for examination, p. 748; Precautions, p. 749; Care and preparation of slides and cover-glasses, p. 749; Making the blood smear, p. 749; Fixation of dried preparation, p. 750; Examination of fresh blood, p. 750; Examination of the stained specimen, p. 751:—Staining solutions, p. 751; Wright's modification of Louis Jenner's stain, p. 751; Technic of staining, p. 751; Results, p. 752; Ehrlich's triacid stain, p. 752.

Hemoglobin, p. 752.—Tests for hemoglobin, p. 752;—Tallqvist's hemiglobinometer, p. 752; Dare's hemoglobinometer, p. 752; Von Fleischel's hemoglobinometer, p. 753; *Hemoglobin estimation by specific gravity*, p. 753; *Oliver's hemoglobinometer*, p. 753; Gower's hemoglobinometer, p. 753; Sahli's hemoglobinometer, p. 753.

The universal microcolorimeter, p. 754; Directions for estimation of hemoglobin, p. 756; Care and use of pipettes, p. 756; Palmer's method of hemoglobin determination, p. 757.

The blood-cell count, p. 759:—The red count, p. 759; The leukocyte count, p. 761.—Many types of blood counters, p. 762:—The Thoma-Metz hemocytometer, p. 764; Oliver's hemocytometer, p. 765; The hematocrit, p. 766.

Leukocytosis and lymphocytosis, p. 766:—Differentiation of leukocytosis from leukemia, p. 766; Average normal leukocyte count, p. 766; Physiologic leukocytosis, p. 767; Preagonal leukocytosis, p. 767; Leukocytosis of pregnancy, p. 767; Leukocyte count in new born, p. 767; Leukocytosis of disease, p. 767; Definition of leukopenia, p. 768; Lymphocytosis, p. 768; Eosinophilia, p. 769; Blood-platelets, p. 769; Counting the blood-plates, p. 769; Determination of hemolytic resistance, p. 770; Total blood volume, p. 770; Coagulation time, p. 771.

Definition.—Obviously, the general term "Diseases of the Blood" must cover diseases affecting the tissues comprising the blood-building and regulating mechanisms. In most instances the blood itself is not diseased but shows a departure from the normal in the numbers and proportions of the different cells contained in it and a shortage, or, in rarer instances, an excess of blood coloring matter in the individual erythrocyte.

In other instances cells wholly abnormal, or cellular elements normal in the blood-building tissues but alien to the blood stream in health, appear and have a direct or indirect bearing upon diagnosis and treatment.

Functions of the Blood.—The life of human tissues is dependent upon the nutriment carried to the living cells by the blood stream, the removal of effete waste products or specific toxins, the maintenance of the vital chemical exchanges indispensable to normal functional activity and the supplying of stimuli, whether chemical or physical, such as are necessary to the normal processes of human life.

It follows that any decided impairment of the blood itself must affect the tissues adversely to a greater or less degree and that even a temporary derangement of excretory function and chemic balance may affect to a varying extent the entire organism. This statement is especially true as applied to disturbances of the higher regulatory centers or to the tissues in which the internal secretions of the body are developed and elaborated.

On the other hand it must be true also that any systemic disease may affect adversely the blood itself, and this actually occurs to a marked degree in many ailments, acute and chronic alike.

The greatest difficulties surround the study of blood formation and destruction despite a great amount of conscientious study and research during several decades.

Even now the amount of absolutely dependable knowledge with relation to the life cycle of blood-cells is extremely scant and our ideas with respect to the etiology of this group of diseases are extremely vague.

A great amount of dependable and valuable knowledge has been attained but theoretic assumption, assertion unsupported by substantial proofs, a vast amount of indeterminate research and an ineradicable tendency both to hair-splitting and complex terminology and to multiple individual classifications make it necessary to avoid in an article of this kind any extended discussion of the vast literature dealing with these problems.

On the other hand, we find on the clinical side a sufficiency of well-proven facts to enable the practitioner to recognize and treat those diseases of the blood properly entitled to individualization.

Importance in Diagnosis.—Aside from the detection of the various anemias and leukemias an examination of the blood properly made in the given case may be the sole exact means of determining the presence or absence of syphilis, typhoid fever, malaria, relapsing fever, filariasis, trypanosomiasis, Malta fever, and many other diseases. The corroborative value of leukocyte counts in cases of pneumonia, appendicitis, and septic infections, acute and chronic, is universally known and accepted, be the testimony affirmative or negative, the count itself excessive or significantly low. Indeed a leukopenia may be as valuable diagnostically as a leukocytosis, especially as a means of exclusion.

Morphologic *vs.* Chemical and Physical Examinations.—The dominant procedure and that chiefly available and most valuable to the practitioner of medicine is the morphologic examination. The physical and chemical examinations though interesting, full of promise for the future, and of definite value in certain instances, do not lend themselves for the most part to the use of the busy practitioner and on the whole have been relatively unproductive up to the present time.

To discuss these in detail or deal with problems of infection and immunity in this section would be going far afield. Nevertheless, certain of the chemical and physical properties of the blood and the fundamental factors in blood formation, destruction and regeneration will be described, inasmuch as these must have a place in the clinical picture of certain diseases of the blood itself and the blood-forming organs herein described.

Finally, we should not lose sight of the fact that little information of value can be obtained through an examination of the blood save by accurate and painstaking work on the part of the physician. A thorough laboratory training is a distinct advantage and absolutely necessary to the man who proposes to deal with the finer methods, but fortunately the more valuable procedures are relatively simple, readily taught and mastered, and can be applied by any conscientious physician who will devote the time necessary to the acquisition of the necessary procedures.

Any one wishing to deal seriously with serology or the refinements of blood pathology must refer to some of the many admirable special books and monographs dealing with these interesting but difficult and complex subjects. This section deals only with diagnostic procedures such as are of direct clinical importance and ready availability.

Commonly Used Terms.—*Anemia* represents a deficit in hemoglobin, erythrocytes, or total volume of the blood. With localized anemia we are not concerned in this section.

Oligocythemia,—red cells below normal in number per cubic centimeter of human blood.

Oligochromemia,—an abnormally low hemoglobin percentage.

Oligemia,—deficiency in total blood volume. This may occur temporarily in severe hemorrhage, more persistently as a result of repeated severe hemorrhages and also in the hemolytic, cachectic and inanition anemias of the more serious grades.

The total volume of blood in relation to body weight is still in some doubt. According to Haldane's method it is one-twentieth; according to the method of Keith and his coworkers, it is found to vary from one-eleventh to one-thirteenth of body weight.

Hydremia,—this state represents a disproportionate amount of water in the blood either from a loss of solid or from an actual increase in liquid content. Normally the water content of the blood is maintained at a level of remarkable constancy. It would be readily understood that temporary increase must occur frequently even under normal conditions such as the ingestion of large amounts of water. A decrease in the amount, of course, occurs under any conditions involving a concentration through loss of water or inability to ingest normal quantities.

The vascular mechanism readily regulates the proportion under ordinary conditions. In disease the mechanism by which this is brought about is oftentimes less well maintained and may suffer serious damage and function most imperfectly. Severe acute hemorrhage may involve a very great loss of water, but as a rule this is repaired very quickly.

The best marked cases of hydremia occurring commonly in practice are those associated with Bright's disease, or serious cases of heart disease with failing compensation and the presence of edema, concealed or frank.

Erythrocytosis (polycythemia),—this term covers the appearance of an excessive number of erythrocytes in a given blood. When associated with an enlarged spleen, marked tendency to cyanosis and greatly increased blood volume, it constitutes an erythremia, which has been known as Vasquez's disease or Osler's disease.

Anisocytosis represents an excessively marked variation in the size of the erythrocytes present in a given blood.

Poikilocytosis is a term applied to abnormal variation in the form and outline of the individual erythrocytes.

Plethora indicates excessive blood volume. The most typical example of true plethora is found in the relatively rare disease referred to above, known as erythremia, in which the number of red cells and total blood volume increase represent double the normal figure. In chlorosis, one of the commonest forms of anemia, there may or may not be an increase in the total blood volume.

Leukocytosis consists of an increase in the number of white cells present in a given volume of blood and the term is applied commonly to an excess of the polymorphonuclear type without abnormalities in ratio as affecting other cells or the presence of abnormal leukocyte forms.

Leukopenia describes a condition exactly opposed to leukocytosis, namely, an abnormally low leukocyte content in a given blood.

Lymphocytosis is an increase in the number of lymphocytes contained in a given volume of blood.

Eosinophilic leukocytosis represents merely an increase in the number of eosinophil cells contained in a given quantity of blood, and "*basophilia*" represents in like manner an absolute increase in these peculiarly modified white cells in a given specimen.

In relative leukocyte increases *(leukocytosis)*, the numbers of any form of white blood-cells may be increased beyond the established normal ratio as determined by a differential count of the leukocytes present. In all cases one should state clearly, therefore, whether any form of leukocyte increase determined is absolute or relative only.

Erythrocytes.—The erythrocytes (red blood-cells) occur in the bone marrow as mononuclear cells irregular in form and staining, "erythroblasts" which may appear as such in the circulating blood in certain diseases, notably in pernicious anemia of the Addisonian type, leukemia, and certain posthemorrhagic states. Normally, however, the nucleus disappears by absorption before the cell reaches the blood stream, undergoing a sequence of changes consisting of (*a*) diffusion of the nuclear chromatin, (*b*) nuclear contraction and pyknosis, (*c*) fragmentation, and (*d*) absorption into the cell body.

THE RED BLOOD-CELL.—Each cubic millimeter of human blood should contain from 4,500,000 to 5,000,000 erythrocytes, the former number representing the average normal for the female, the latter that for the male. A fluctuation of half a million cells may be assumed as within normal limits.

The average size of the normal erythrocyte is 7.5 μ, but there is a permissible normal variation, varying from 6.5 to 8.5 μ. The microcyte measures from 3 to 5 μ, and the megalocyte from 9 to 20 μ. The latter form is especially common in anemias of the pernicious or profound secondary type, and in most cases of Addisonian pernicious anemia the diagnosis may be suggested by the dominance of the large forms even before megaloblasts or marked cell deformity (poikilocytosis) appear.

In the circulating blood the erythrocytes appear as bi-concave, non-nucleated discs, nearly uniform in size and outline, and, under normal conditions, show a universal and equal affinity for the acid dyes.

Abnormal Forms.—Deformity (poikilocytosis) and great variations in size (anisocytosis) may occur in varying degrees in certain anemias. Such deformities may be bizarre and extreme as observed in (*a*) the marked but not excessive variations encountered occasionally in marked chlorosis of long standing, and (*b*) the extreme diversity of form and size frequently present in pernicious anemia of the Addisonian type. These deformities differentiate readily from the slight variations observed in normal blood.

In childhood, youth and adult life the red bone-marrow is the source of the red blood-cells. The erythrogenetic activity of the liver, spleen and, to a less degree, of other tissues, so notable in embryonic life subsides wholly a few months after birth and is revived only under the abnormal stimulus of excessive blood destruction. In such an emergency the spleen especially may become an active regenerative factor, whereas the liver is excited to renewed activity only in hemolytic anemias of the severest grades.

Evidences of Regeneration.—In any anemia associated with blood destruction, one may find, primarily at least, evidences of an attempt at regeneration which is reflected chiefly in the types of erythrocytes present. The most easily recognizable evidence is that furnished by the presence of immature red cells (blasts), but by special staining methods the presence of an unusual number of reticulated erythrocytes may also be shown.

To demonstrate these one may use a saturated normal salt solution of cresyl-blue, a small quantity being diluted 80 times with normal salt solution and mixed in a white cell counting pipette with the blood under investigation in a proportion of 20 parts of the former to 1 of the latter. This mixture is thoroughly shaken for from three to five minutes when the cells not only will be well stained but also properly distributed. One thousand or more must then be counted to determine the proportion of reticulated cells present in preparations freshly made and ringed promptly with vaseline to prevent drying at the edges.

The presence of reticulated red cells in certain cases may reach 10 per cent. of the total erythrocytes, and Minot states that an undue persistence in the reticulated cell increase after several days, or a renewal of the same phenomenon after subsidence, may be valuable in the detection of concealed hemorrhage. Polychromasia and an increase in blood-platelets also accompany regenerative activity.

Unusual Erythrocytic Staining Reactions.—Especially in myelogenous leukemia and pernicious anemia, but to a less degree in any severe chronic anemic state, one may meet with cells which have lost their normal special affinity for an acid stain and take indifferently both the acid and basic elements of the mixed stain. As a result the color in the stained specimen is often widely variant and irregular, and in the nucleated cell-forms the nucleus as well as the protoplasm may show this characteristic. The greater the deficiency of hemoglobin in the individual cell the stronger is its affinity for the basic element in a mixed stain and hence its tendency to show this polychromatophilia. The so-called "corpuscles of Poggi" are cells which take the basic stain even in fresh unfixed specimens of blood.

THE NORMOBLAST (7.5 to 10 μ).—Reference has been made in a preceding paragraph to the nucleated erythrocytes normal in size or slightly over-size. These have a deep basic staining nucleus which shows a peculiarly sharp definition and a coarse granular structure which occupies usually about half the cell-body; but this may be much smaller and occasionally it is divided or undergoing karyokinesis. Such cells occurring in the blood seem to represent an attempt at blood regeneration and are encountered with special frequency in myelogenous leukemia, pernicious anemia, severe posthemorrhagic forms, and also occasionally in marked cases of chlorosis of long-standing.

THE MEGALOBLAST (11 to 20 μ).—This cell which, as stated previously, has a pathologic significance when present in the circulating blood is readily recognized by its large size and the presence of its nucleus which stains a faint blue or green and shows a fine structure. The nucleus itself is usually large, but occasionally small, and takes the stain as deeply as the normoblast. In contrast to the normoblast it represents defective hemogenesis and indicates degeneration, being found as the prevailing or dominant type of erythroblast only in primary pernicious anemia, nitrobenzol poisoning and certain profoundly toxic cases of bothriocephalus anemia. It is said that an occasional cell of this type may be found in any severe anemia.

THE MICROBLAST (5 to 6 μ).—This small cell with deeply staining nucleus is practically identical with the normoblast but distinguished from it only by its lesser size and possessing exactly the same clinical significance and association.

MESOBLASTS.—In addition to the types of erythrocytes already mentioned, one encounters clinically forms which usually defy exact differentiation and placing. For example, one may encounter cells which may be immature normoblasts and show a pale nucleus with stippling and polychromatophilia in their protoplasm; yet others may be as large as megaloblasts, which show only faint staining of the protoplasm and a deep basic stained nucleus. These variant forms possess in themselves little clinical significance.

BASOPHILIC ERYTHROCYTES.—These cells, occasionally encountered, show fine, coarse, spicular or even ovoid granules regularly or irregularly distributed throughout their protoplasm.

Cabot has described intra- and extracellular ring bodies in cases of lead-poisoning, pernicious anemia and lymphatic leukemia. Da Costa has found these also in the profound anemias of sepsis. These, it is now known, take the acid stain, if Wright's solution is used. The basophilic erythrocytes occur chiefly in lead-poisoning, certain cases of chlorosis, and the Addisonian form of pernicious anemia.

MAURER'S SPOTS.—These irregular, dark violet-red spots of variable size appear in infected red blood-cells in certain cases of estivo-autumnal malaria, require a special stain (Maurer's modification of the Romanowsky) and are without any clinical significance or importance.

SCHUFFNER'S STIPPLING ("SCHUFFNER'S SPOTS").—These are minute dark red dots which may be detected in infected erythrocytes of tertian malaria but lack all specific clinical importance.

HOWELL'S BODIES.—Howell, in 1891, described as occurring at times in the nucleated red cells certain peculiar, round, sharply defined bodies, usually single but in rare instances multiple, which stain precisely as nuclear substance does, and occur chiefly in blood crises and in the normally staining nonpolychromasic cell. They are quite unlike, and distinct from the nuclear fragments often encountered in many forms of anemia in which erythroblasts appear. These are the bodies so generally and mistakenly described as "Jolly bodies" or less frequently as the "Howell-Jolly bodies," but were not described by Jolly until 1908, seventeen years after they had been reported by Howell. They occur with special frequency after splenectomy and by many are regarded as nuclear fragments.

The Leukocytes.—NORMAL LEUKOCYTIC FORMS.—There are six recognized normal leukocytes, namely, (*a*) the polymorphonuclear neutrophils which constitute from 60 to 75 per cent. (average 70 per cent.) of the total leukocytes present in a given amount of blood; (*b*) the small lymphocyte, constituting from 20 to 25 per cent. (average 20 per cent.); (*c*) the large mononuclear leukocyte averages 5 per cent. of the total leukocytes present in a given specimen; (*d*) the transitional forms (2 to 4 per cent.); (*e*) the eosinophils, usually varying in number in the given specimen between 0.5 per cent. (average 5 per cent.); and (*f*) the basophil or "mast" cell constituting ordinarily from 0.1 to 0.5 per cent. of the total leukocytes.

(*a*) *The Polymorphonuclear Neutrophil.*—This cell measures from 7.5 to 12 μ, averages about 11 μ, and is characterized by its irregular lobulated nucleus, staining dark blue and connected by chromatin strands, and the presence of neutrophilic granules in the protoplasm which take a lilac or pink color with Wright's stain.*

(*b*) *The Small Lymphocyte.*—This measures from 5 to 10 μ, and contains a single round deep-staining nucleus almost filling the cell and often obscuring the border of protoplasm, the latter being almost wholly unaffected by the triple stain, but colored sky-blue, if the Romanowsky method be employed.

(*c*) *The Large Mononuclear Leukocyte.*—This measures from 10 to 15 μ, and carries a round or oval nucleus straining pale blue, and a relatively large amount of protoplasm.

(d) *The Transitional Leukocyte.*—This differs from the large lymphocyte only in lacking the indented crescentic or reuniform nucleus of the latter.

(*e*) *Eosinophils* (8 to 11 μ).—These are readily recognized by their coarse, acid-staining granules and polymorphonuclear type. The granules are especially brilliant in certain parasitic infections and septic conditions (Gulland).

(*f*) *Basophils* [*Mast Cells*] (7.5 to 12 μ).—The distinguishing feature of the basophil cell is the presence of its fine, basic-staining granules.

---

* Ehrlich's triacid stain is also very effective. In general, a mixture of an acid and basic dye is requisite.

The nucleus is polymorphous and stains a pale green with the eosin and methylene-blue mixtures. The characteristic granules are best shown by Wright's stain or that of Leishman and not at all by the triple stain.

UNUSUAL OR ABNORMAL FORMS.—The *myelocytes* [marrow cells] (15 to 20 μ) are large immature forms of the granular leukocytes and may contain neutrophilic, eosinophilic or basophilic granules, thus constituting three sub-varieties. They are the dominant cells of the normal bone marrow.

The nucleus is spherical or oval, tends to be eccentric, poor in chromatin, staining feebly or moderately with the blue, occasionally shows division and often a marginal light circle.

The presence of the granules distinguishes the myelocyte from the myeloblast and large mononuclear forms and the lack of lobulation or twisting of the nucleus from the polymorphonuclear cell. Occasionally it is slightly indented.

With Wright's stain the neutrophilic myelocytes show lilac or pink granules with a purplish admixture. Eosinophilic myelocytes show the ordinary coarse, brilliant, eosinophilic granules, occasionally showing some basophil admixture.

Significance.—The cell is invariably pathologic, occurring in many cases of profound anemia or excessive leukocytosis, occasionally in lymphatic leukemia and Hodgkin's disease, but only in small numbers, whereas in myelogenous leukemia they are the most characteristic and predominant of the white cells.

The Metamyelocyte.—This represents a transitional stage between the myelocyte and the transitional form of the polymorphonuclear leukocyte. The cell is relatively small, the nucleus is more strongly basophil and gives evidence of beginning segmentation. It is present only in association with the myelocyte.

The Myeloblast.—This scanty or non-granular form, dominant in embryonic myeloid tissue, probably the mother cell of the *granular* (marrow) myelocyte, differs from the large lymphocyte morphologically, chiefly in the following particulars (Naegeli):

(*a*) *Constant* absence of the clear perinuclear zone.

(*b*) Decided differences in nuclear form and structure.

(*c*) Greater number of nucleoli.

(*d*) In strongly heated specimens stained with methylene-blue the lymphocyte nucleus is pale and shows one or two nucleoli very distinctly; the myeloblast nucleus is stained intensively and does not show its nucleoli (two to six).

The greater chromatin content of the myeloblast nucleus is also evident if the triacid stain is used. Small forms are occasionally encountered. Naegeli strongly recommends the use of the Schridde-Altman staining process for differentiation. This is a tedious and prolonged procedure, the technic of which is to be found in Naegeli's book or some of the recent works devoted wholly to this branch. These cells are rarely present save in the crises of myeloid leukemias and perhaps pernicious anemia and the infantile forms.

Promyelocytes.—These represent a transition form between the myeloblast and the myelocyte. The nucleus is large and poor in chromatin; nucleoli are present (none visible in fully developed myelocyte) and the protoplasm is strongly basophilic and contains a few small, scattered granules.

Türck's Irritation Forms.—These are large cells, probably identical with the "pathologic" myeloblast, containing absolutely no granules in their protoplasm, usually showing vacuoles, especially likely to appear during an acute infection and of little or no clinical importance or significance.

Giant Marrow-cells (Megakaryocytes.)—These important elements, progenitors of the blood-platelets, are huge cells with large convoluted nuclei. Their occurrence in the blood is rare, accidental and extremely brief, as they cannot pass the capillaries.

Lymphoblasts.—A replica of the small mononuclear cell in its morphology, but the equal of the large mononuclear in size, is found occasionally in the blood of normal children and in the adult suffering from disease.* It is important only because confusing, when the possibility of its presence is not known.

The Schridde-Altman granules are merely acidophil granules within the leukocytes brought out by the use of the special stains of Schridde or Freifeld and have no special clinical value or significance.

"Azure granules" within the lymphoblast protoplasm are said to be inconstant in ordinary leukemia of the lymphatic type but constant in the acute form. They are developed best by the Giemsa or Wilson stain and so shown occur only in the *small lymphocyte* as *red* granules.

Giant Lymphocytes (Pathologic Lymphoblasts).—These abnormally large cells carry a round nucleus, poor in chromatin, staining but slightly with methylene-blue or the triacid stain, somewhat better with eosin-hematoxylin and showing very clearly its nucleoli. This form includes the cells with lobulate nuclei described by Rieder, but in these there exist only deep fissures or indentations (Naegeli). Such cells may constitute the dominant type in acute leukemia, and usually indicate an extremely rapid and malignant type of case (Sternberg-Naegeli).

Melanemia.—Pigmented leukocytes occur in cases of melanotic sarcoma and, in malaria, free in the blood, during the segmentation stage of the disease.

Idiophilia.—If a dry but unfixed smear be *gently* pressed down upon a generous drop of specially prepared iodin and potassic iodid solution,** the normal blood-cells take a uniform yellow tint, but in *septic conditions* both intra- and extra-cellular brown granules are seen or a diffuse protoplasmic staining occurs, especially affecting the neutrophilic leukocytes and, rarely, the basophils and myelocytes.

The reaction is *reasonably constant* in septic conditions *(not in pure tuberculous abscesses)*, but is present in many other diseases, such as purpura hemorrhagica, acute miliary tuberculosis, certain typhoids and malignant disease. It is of genuine value in the differentiation of septic from non-septic effusions and joint diseases.

Perinuclear Basophilia.—Neusser's perinuclear basophilic granules occurring in specimens submitted to the triacid stain were regarded by him as indicating the uric acid diathesis, but now are proven to be artefacts and of no diagnostic significance.

The Inclusion Bodies of Döhle.—These may be found in the blood smears of patients suffering from scarlet fever and in several other acute infections (syphilis, measles, erysipelas). They are readily detected under simple staining with Loeffler's methylene-blue, as coccus-like, irregular, rod-like or crescentic bodies lying usually within the polymorphonuclear leukocytes.

---

* Probably the parent cells of the normal "large mononuclear leukocyte," and lymphocyte.

** Iodin 1, potassium iodid 3, water 100, gum Arabic 50.

Plasma-cells.—These may reach the circulation in congenital hemolytic jaundice, multiple myeloma and leukemia, though normally encountered in small numbers only in the bone marrow, lymph glands, spleen and connective tissue. Pathologically they are associated with the granulomata and are especially prominent in syphilitic lesions. They are strongly basophilic and granular, often triangular in outline and the single nucleus of the "wheel-spoke structure" is small and eccentrically placed. A perinuclear zone is invariably present in these cells.

Essential Laboratory Procedures.—In connection with the so-called blood diseases the following tests are essential:

1. The determination of hemoglobin percentage.
2. The red cell count.
3. The white cell count.
4. The examination of fresh blood.
5. The examination of smear preparations: (*a*) stained; (*b*) unstained.
6. The blood-platelet count.

The study of the agglutination reaction in infections, the examination of the exudates, complement-fixation tests, the determination of the coagulation period, specific gravity determinations, estimation of blood volume, viscosity tests and cryoscopic precedures lie outside the scope of this section.

The Coloring Matter of the Blood.—The normal arterial blood derives its characteristic bright red color from the hemoglobin contained in its erythrocytes and combined loosely with about 21.6 per cent. by volume of oxygen which forms oxyhemoglobin. The red cells contain also about 13 per cent. by volume of CO_2. The blood-plasma normally contains about 26 per cent. by volume of CO_2 and the normal content of venous blood is approximately 48 per cent. by volume. Proper oxygenation of the blood is vital to normal existence and practically all forms of clinical dyspnea encountered are due to oxygen deficit.

Inasmuch as the ability of the red blood-cell to take up oxygen depends upon the amount of this proteid substance, hemoglobin, whose peculiar characteristic is the avidity with which it forms unstable compounds with oxygen, it can be seen readily how important determinations of the proportion of this substance in any given blood become in clinical practice.

In the commonest form of anemia (chlorosis) it is the poverty of the individual erythrocyte in hemoglobin which makes the diagnosis absolute. In all forms of anemia the ratio of the contained hemoglobin to the established normal constitutes one of the important factors as affecting both diagnosis and prognosis.

A rough estimate of the percentage of hemoglobin may be made from the appearance under the microscope of the ordinary stained or unstained smear preparation but for accurate work several forms of special apparatus have been devised. By means of these the given specimens of blood, either whole or in a known degree of dilution, are compared with a fixed color scale upon which the figure 100 represents a full normal value and from which the hemoglobin percentage shown by the blood under examination can be determined more or less accurately.

Technic of Blood Examination.—TO OBTAIN BLOOD FOR EXAMINATION. —It is essential that the actual technic should be thoroughly understood, and intelligently and expeditiously carried out.

PRECAUTIONS.—One should not trust to the flow of blood for sterilization either of the skin or of the instrument employed. The ear lobe or the finger-tip should be carefully cleansed with alcohol, bay rum, or some similar substance always available, and *the needle or lancet used should be sterilized in the flame.*

The patient may be asked whether he "bleeds easily" or the reverse with a view of determining the size, depth of the puncture, and avoidance of serious complications in cases of hemophilia. Two patients of this type in the author's clinic bled steadily for several hours from a very minute puncture.*

For making the puncture an instrument with a sharp cutting edge should be used. The Hagedorn needle or the *spring lancet with a trocar point* is most suitable, the ordinary needles being poor substitutes. Some workers prefer to use a suitable piece of broken cover-glass which is firmly grasped between the finger and thumb at the point required to permit necessary penetration and at the same time limit the depth of the puncture. If quickly and smartly done the stroke is almost painless and the resulting blood-flow free.

The puncture itself should be sufficiently free and deep to obviate *squeezing or excessive friction,* and, furthermore, the instrument should permit a quick, painless stroke** and the first two or three drops should be discarded. *The blood should flow spontaneously and, to maintain it, light brisk friction serves admirably, but pressure should never be employed.* To check it, firm, steady pressure is sufficient, or in the case of the finger, vertical elevation of the arm.

An edematous area or one in which local cyanosis is marked should be avoided in obtaining specimens for examination. The former yields a diluted blood, the latter a misleadingly concentrated specimen.

CARE AND PREPARATION OF SLIDES AND COVER-GLASSES.—All material should be of the best sort, seven-eighth inch square cover-glasses being superior to the round; both these and the slides should be *thin.* When received from the dealer, they should be thoroughly washed in soap and water and then placed in the following solution: Hydrochloric acid 1 part, absolute alcohol 29 parts, water 70 parts, or they may be placed in solution containing equal parts of alcohol and ether. When required, they should be wiped thoroughly, polished with tissue paper or with soft linen, and, if convenient, passed through a flame. A small drop of blood will spread satisfactorily and evenly between a perfectly clean slide and its cover-glass or between two cover-slips, especially if these are slightly warm.

MAKING THE BLOOD SMEAR.—To make a good smear preparation one may use either cover-glasses or slides, but these must be absolutely clean and dry and the utmost care must be observed to make no pressure such as may result in deformity or fracture of the blood cells. If two cover-glasses are used a small drop of blood at the point of puncture should be lightly touched by one, the other placed quickly and gently upon it, allowed to remain an instant to permit the spread of the blood between the two surfaces, and then separation of the two effected by a sliding (not a lifting) movement, all downward pressure being avoided. This last precaution may be readily observed if the two slides (before being put together) are placed the one at right angles to the other so that in sliding them apart the corners may be held by the fingers or forceps. The glass surface upon which the spread is to be made should never be allowed to touch the skin of the patient.

---

* As a matter of fact the risk of any serious or fatal hemorrhage is practically negligible.

** Blood may be taken from young children in this way without arousing them from sleep.

If slides are used, a drop may be taken in the same manner upon one slide; the short edge of another allowed to rest upon the surface beyond the point where the drop of blood lies and the other end supported by the finger of the observer; that is to say, the second slide rests obliquely upon the first and is pushed over the drop of blood without any pressure save that represented by its own weight.

There are various other methods which may be used, but these two are sufficient and satisfactory.

A good smear should show the cells evenly distributed throughout large areas and should not look to the eye smeary or thick. If carefully preserved the dry unstained specimen will keep for months. Forceps are not needed at any stage of the procedure, but the stained preparations are more brilliant if the slip is immediately, though slowly and carefully, dried above a flame.

Nothing but persistent and painstaking practice will enable one to make good smears but the result is well worth the time and labor expended.

FIXATION OF DRIED PREPARATION.—The use of the self-fixing Wright stain makes a prolonged description of the older methods unnecessary. Smears may be "fixed" for rapid work with the old triple stain by any one of four simple methods: (1) *Passing the cover-slip through a small flame three or four times;* (2) *boiling one minute in absolute alcohol;* (3) *immersion for one minute in a 1 per cent. alcoholic solution of formalin;* and (4) *exposing smear for a few seconds to formalin vapor.* The older "heating" methods are delicate, require for good results a special oven or heating stage, and are not necessary for ordinary clinical work.

EXAMINATION OF THE FRESH BLOOD.—Fresh blood is readily examined by allowing a small drop to spread evenly under a perfectly clean, moderately warm, cover-slip and slide. This procedure is valuable in the observation of (*a*) *leukemia;* (*b*) *malarial organisms* (and their ameboid movements if the stage is kept warm);* (*c*) *filaria;* (*d*) *relapsing fever;* (*e*) *trypanosomiasis;* (*f*) *rouleaux formation;* (*g*) *increase of fibrin;* (*h*) *increase of blood plaques;* (*i*) *low color index;* (*j*) *approximate number of red and white cells;* (*k*) *cell deformity;* and (*l*) *wide departure from normal coagulation time.*

Nucleated red cells are not thus revealed and the rough count of leukocytes made possible is not dependable. If the cover slip edges are sealed with a little vaseline, one may preserve the fresh specimens for hours.

Hemoconia.—The presence of the mysterious and clinically negligible "blood dust" or hemoconia is indicated by a rapid vibration of these tiny colorless, highly refractile, unstainable bodies, which may be fat particles, nuclear or cell fragments or extruded granules.

---

* Brownian movement and the contractions preceding crenation and cell death can hardly be confounded with the true ameboid movement.

Fibrin.—Increase or decrease of fibrin and rouleaux formation may be determined roughly after the specimen has stood for ten or fifteen minutes. No smear is made, but the cover-glass lightly touches the blood drop and is then placed upon the slide. The stage should be dimly illuminated to show the fibrin threads which frequently radiate from groups of blood-plates.

Fibrin is increased in pneumonia, acute rheumatism and various septic infections and diminished in leukemia and pernicious anemia, typhoid fever, malaria, measles, variola, Graves' disease and various conditions associated with extreme inanition. In general the fibrin increase (hyperinosis) occurs in diseases in which leukocytosis is present, though in leukemia itself a diminution (hypinosis) occurs.

EXAMINATION OF THE STAINED SPECIMEN.—Modern staining methods depend upon the selective affinity shown by the different constituents of the cellular elements of the blood for certain anilin dyes, which are divided into three groups: (*a*) *Basic,* (*b*) *acid,* (*c*) *neutral.* By using combinations one may in a single step attain differentiation. *The basic dyes,* such as methyl-violet, methylene-blue or hematoxylin (chromatin stains) act chiefly upon nuclei. *Acid dyes,* such as eosin, orange G. or acid fuchsin are protoplasm stains, while *neutral dyes* (resulting from the mixture of acid and basic colors in solution) color beautifully the "neutrophil" granules of the leukocytes.

Staining Solutions.—Ehrlich's triacid or triple stain now has been displaced by Wright's modification of Jenner's stain, an alkaline eosinate of methylene-blue, which, *by at once fixing and staining the specimen,* eliminates the laborious and delicate heating process of the older method.

Wright's Modification of Louis Jenner's Stain.—The student or practitioner had best purchase the "soloid" tablets[*] or procure a solution ready-made through some drug supply house, as the formula is somewhat complex.[**] It should be tightly corked to prevent precipitation.[***]

Technic of Staining.—(1) *The dried but unfixed smear is completely covered with the stain for one minute.* (2) *Distilled water is added to the stain on the cover-slip drop by drop until a greenish metallic scum appears and the margins show a reddish tint.* (3) *After three minutes the stain is washed off with water, leaving a purplish specimen, which is washed until the film is yellowish or pink.* (4) *It is gently dried between filter paper.* (5) *Then it is mounted in balsam.*

[*] The "soloid" tablets of Burroughs, Wellcome and Company offer a ready method of making up fresh stain. One soloid is triturated with 10 c.c. (2.71 fluidrams) of pure methyl alcohol, the dissolved stain decanted and the undissolved stain again extracted with another 10 c.c. of alcohol. This process is repeated a third time so that 30 c.c. (1 fluidounce) in all is used. The stain should then be passed through a filter.

[**] FORMULA.—(*a*) Make a 0.5 per cent. aqueous solution of sodium carbonate, place in Erlenmeyer plaque, add 1 per cent. of Grubler's medicinal methylene-blue; place in steam sterilizer for an hour. (*b*) After cooling, add while stirring with glass rod, a 1-1000 aqueous solution of Grubler's water-soluble yellowish eosin until the color of the original mixture changes to purple and presents a lustrous yellowish scum upon its surface. (About ⅛ as much eosin solution as methylene-blue solution will be found necessary.) (*c*) Collect this scum by filtration, dry it, and with it saturate methyl alcohol (100 c.c. [3.38 fluidounces] of the latter will dissolve about 3/10 of a gram of the dry precipitate). (*d*) Filter and add 25 per cent. of methyl alcohol. The stain is now ready for use and, if kept tightly corked, should neither precipitate nor show impairment though kept for a long period.

[***] The Giemsa stain is another Romanowsky modification of great value, but does not yield the best results with neutrophilic granules. T. M. Wilson's stain, yet another Romanowsky modificaion, is used in many laboratories, but has no decided superiority to Wright's modification of the Jenner stain.

Results.—The appearance of the various cellular elements is as follows: The *erythrocytes* are orange or pink throughout. *Erythroblasts* show deep blue nuclei, *neutrophil granules* lilac, *eosinophil granules* pink, fine *basophil granules* a deep blue stain, *bacteria* and such organisms as malarial parasites blue. *Myelocytes* show a purplish or dark lilac nucleus and reddish or dark lilac granules.

Ehrlich's Triacid Stain.—*The ready-mixed powder* for making this stain may be bought of any drug supply house and the student or practitioner should not attempt to make the original.*

Fairly good rapid work may be done with a good triple stain in the absence of Wright's stain by heating the smear carefully as in the staining of tubercle bacilli and staining for thirty seconds or less, washing, drying and mounting (Cabot).

Other heat fixation methods are now so little used that a description is not deemed necessary. Scott fixes by a few seconds' exposure to formalin fumes before applying Jenner's stain and shows beautiful results.

Hemoglobin.—Hemoglobin or, more properly, oxyhemoglobin constitutes about nine-tenths of the bulk of the red corpuscles. It is a proteid substance containing 4 per cent. of hemochromogen, an iron-holding body, and 96 per cent. of concentrated, almost insoluble albumin *which readily forms unstable compounds with oxygen.* The great value of its determination by clinical tests may be readily appreciated.

TESTS FOR HEMOGLOBIN.—*An expert observer can make a rough estimate of the percentage of hemoglobin from the appearance of the ordinary stained or even the unstained smear preparation, but for accurate work several forms of apparatus have been devised, all depending upon a comparison of a given specimen of blood, either whole or in a known degree of dilution, with a fixed color scale.*

Tallqvist's Hemoglobinometer.—*This, the simplest and least reliable,* consists of lithographed color hands. Each has a central perforation and represents the color of blood in dilutions running from 10 per cent. to normal.** A drop of the patient's blood is taken up by the absorbent paper and the resulting stain is placed under the central perforation of the color bands and comparison is made *as soon as the stain has lost its wet gloss, not after complete drying.*

This is a simple, rapid, but *inaccurate* method, permitting an error of at least 10 per cent., and the color scale fades, if not kept from the light. It is distinctly inferior to Dare's instrument which takes hardly a minute more of time.

Dare's Hemoglobinometer.—A circular disc of tinted glass, representing variations in blood-coloring matter of a known degree, is brought into direct contrast by transmitted candle light with a film of the fresh whole blood drawn by capillary attraction between two glass plates, one transparent, the other translucent and white. A detachable observation tube and a circular shield protect the eyes from extraneous light, and the percentage of hemoglobin may be read directly from the scale. This excellent instrument may be used in daylight if pointed at some dark object, and its readings are not materially affected by an excess of leukocytes.

---

* FORMULA.—Ehrlich-Biondi powder, grains xv (.972 gram); alcohol (*absolute*) 1 c.c. (16 minims); and distilled water, 6 c.c. (1.62 fluidrams).

** The color scale is bound with 50 sheets of special paper, each divisible into three parts, furnishing material for 150 tests.

Von Fleischl's Hemoglobinometer.—This well-known instrument, or its more accurate modification, has been largely superseded by the simpler and cheaper instrument of Dare. If it is used one should procure Miescher's modification. The following precautions are necessary to good results:

(a) The capillary tubes for taking the drop must be absolutely clean and should be tested out for equality of calibration when purchased.

(b) All blood must be removed from the surface before mixing, leaving the caliber exactly filled.

(c) The blood must be taken quickly, washed out into the chamber, and thoroughly mixed in the shortest possible time.

(d) The observer should face the end of the movable colored wedge with the thumb-screw on his right.

(e) Decision as to color should be made quickly to avoid uncertainty and confusion.

(f) The thumb-screw should be sharply turned in order to obtain as vivid a contrast as possible until the final match of color is achieved.

(g) Should the blood solution appear turbid and lack proper color, as in the case of leukemia, add a few drops of a dilute aqueous solution of potassium hydrate.

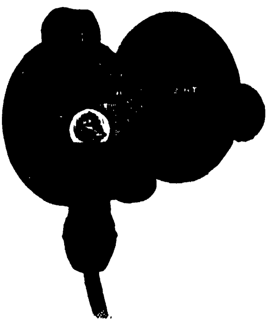


FIG. 1.—DARE'S HEMOGLOBINOMETER.

(h) Where the hemoglobin is below 30 per cent., double or treble the usual amount of blood should be used, the percentage obtained being divided proportionately.

(i) The examination should be made in a dark room, or by means of a light-proof box by candle light, and in any case some form of tube should be used for observation, a simple roll of black paper being ordinarily sufficient.

Hemoglobin Estimation by Specific Gravity.—By use of the tables to be found in all the larger works dealing with this subject the hemoglobin present in a given specimen may be very accurately estimated by Hammerschlag's modification of Roy's method. The procedure is too cumbersome and fussy to be recommended to the practitioner and will not be described.

Oliver's Hemoglobinometer.—This instrument depends upon the scale of colors based upon diluted blood. It has no advantage over the two preceding methods.

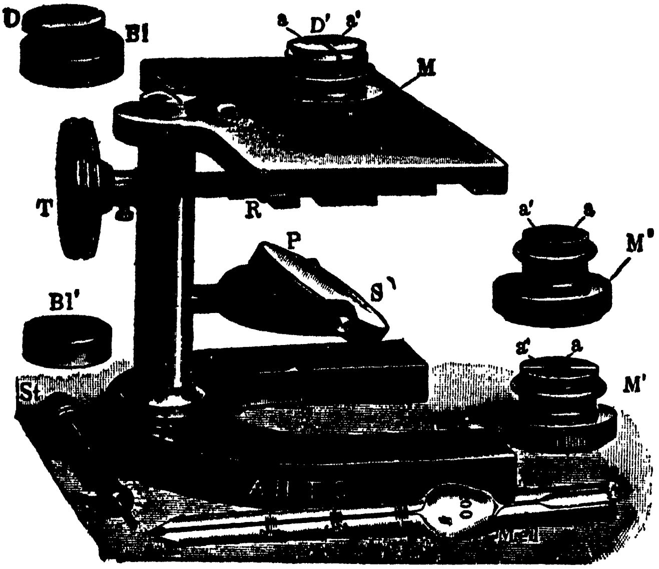
Gower's Hemoglobinometer.—This little instrument has the merit of extreme simplicity, yet in practice one may lose more time by its use than with the other more elaborate instruments, inasmuch as a slight error in dilution means a repetition of the whole process.

Sahli's Hemoglobinometer.—This admirable instrument resembles Gower's hemometer, but is well adapted to quick, accurate work. ***The empty graduated tube is filled to the mark 10 with a decinormal solution of HCl which is saturated with chloroform. The blood is then added by*** *means of a measuring pipette and the mixture made thorough and complete. Finally, after mixing for exactly one minute, distilled water is added, guttatim, until the color corresponds to that of the control tube which contains an acid hematin solution.*

The color comparison is easy and definite, but 90 should be considered an average normal and the instrument should be kept in its case or in a dark place and inverted once or twice before using.*

The author believes that the hemometers of Dare and of Sahli best combine simplicity with adequate clinical accuracy.

The Universal Microcolorimeter.—Dr. Theodore Kuttner of New York has devised a pocket size colorimeter which apparently is well adapted to several procedures chief of which are (*a*) the hemoglobin test, (*b*) the estimation of glucose in the blood by a modification of Benedict's method,



Courtesy of A. H. Thomas & Co.

FIG. 2.—VON FLEISCHEL'S HEMOGLOBINOMETER (MIESCHER'S MODIFICATION).

Description.—Milled wheel at left (*T*) moves a tinted glass wedge (*R*) under the fixed metal stage surmounted by double chamber reservoir which received light from the calcium sulphate reflecting disc (*PS*) below. Half of the same chamber is filled with the diluted blood contained in the measuring capillary pipette (*Mel*). The other contains only plain water but receives its light from the colored wedge. By moving the wedge back and forth the colors are matched and the percentage reading is shown on a scale visible through the opening (*M*) just in front of the supporting upright. The blood is obtained in exactly the same manner as for a blood-count, the diluent being calcium carbonate solution (0.1 per cent.) and the tube permitting the observer to use dilutions of 1:200, 1:300 or 1:400 according to the diluting height to which the blood column is allowed to rise (marks 1/1, 2/3, 3/4 respectively) before diluting and thoroughly mixing. Increased accuracy is obtained by the use of a grooved cover glass (*D'*) which fits over the slightly raised partition dividing the two chambers, which must each be so filled as to present a convex meniscus. The necessary narrowing of the field is secured by cap-diaphragm (*Bl'*). The average of at least ten determinations are required for accurate work.

---

* The instrument registers a maximal normal represented by the blood of healthy young Swiss males. Ninety per cent. would represent fairly an average normal.

and (*c*) the phenolsulphonephthalein test.* An abstract of Dr. Kuttner's description is appended covering its application to these three procedures.

(*a*) *Description of the Instrument.*—The same calibrated and color tube employed in the Sahli-Gower hemoglobinometer has been adopted for this instrument. The Sahli allows both the calibrated and color standard tubes to be viewed at full length; the new instrument, however, shows only a small part of the tubes when making color comparisons. This facilitates the color reading and is less fatiguing to the eye. An additional feature is a prism, which apparently causes the contents of the tubes to approach each other more closely, thereby accomplishing greater accuracy in the comparison of colors.

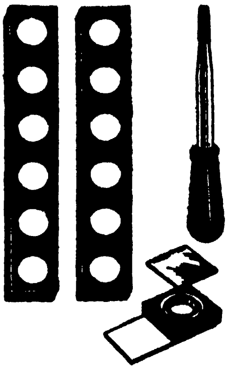


FIG. 3.—OLIVER'S HEMOGLOBINOMETER. The discs shown as white in the illustration are colored to represent the various blood dilutions and direct comparison is made with a solution of the actual blood obtained by a measured mixing capillary pipette furnished with the instrument. Intermediate readings are obtained by placing squares of tinted glass over the fluid under examination.

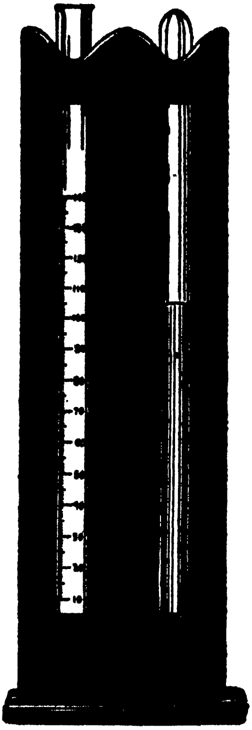


FIG. 4.—SAHLI'S HEMOGLOBINOMETER.

The instrument consisting of a closed upright box (dimensions 2.5 cm. by 8.5 cm. [1 in. by 3½ in.]) is smaller than the Sahli. At the top there are two openings: one for the color tube, the other for the calibrated tube. Near the lower front part is a window provided with the above-mentioned prism (Helmholtz double plates), which serves the purpose of having the colors of both tubes appear close together, forming one continuous color band. The prism is easily removed for cleansing and can be quickly readjusted. A sliding door which can be raised and lowered, protects the prism from dust and injury. The color standard and calibrated tube are separated from each other by a partition, which prevents light from being reflected from one tube to the other.

---

* Journal A. M. A., July 17, 1915, pages 245 and 246; and April 29, 1916, pages 1370-1373.

Directions for the Estimation of Hemoglobin (*Standard Color Tube "Hematin"*=*15 grams* [*231.48 grains*] *Hgb.*=20 c.c. [5.42 fluidrams] O_2).—Into the calibrated tube No. 9 enough of a 1/10 normal solution of HCl is poured to reach the mark 10. With the capillary pipette No. 1 blood is drawn to the 20 cu. mm. mark, the sides of the pipette wiped with absorbent cotton and the blood expelled while dipping the pipette to the bottom of the calibrated tube. Water is sucked up two or three times and these washings added to the tube. This is set aside for from one to two minutes and then compared with the standard color tube in the instrument. Water is added drop by drop, the solution well mixed after each addition, until the color matches that of the standard. When this is accomplished, the percentage can be read off directly by noting the figure which the meniscus has reached on the scale. As percentages occurring much below 50 are liable to error, it is best to use more blood when such anemic cases are encountered. Thus, in order to obtain greater accuracy, two, three or five times the amount of blood should be taken, with capillary pipette No. 2, also twice the amount of 1/10 normal HCl and the same process should be followed, but the result must be divided by two, three or five.

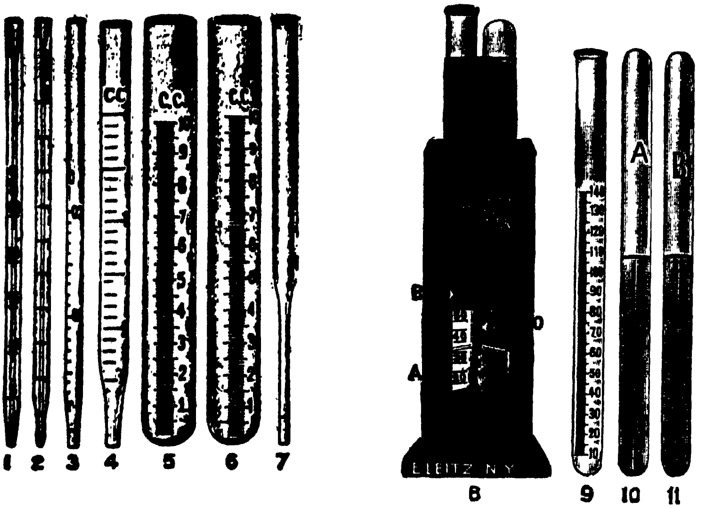


FIG. 5.—KUTTNER'S POCKET-SIZE COLORIMETER.

Care and Use of the Pipettes.—Four pipettes are furnished with the instrument No. 1, up to 25 cu. mm.; No. 2, 1/10 c.c. divided into ten divisions; No. 3, 2/10 c.c. divided into ten divisions; No. 4, 2 c.c. divided into ten divisions. Pipettes must be clean and dry before use.

When the required amount has been drawn into the pipette the tip of the tongue should be placed against the mouthpiece attached to the rubber tubing of the pipette. Before expelling the contents, the pipettes are held in a horizontal position and wiped with absorbent cotton. After use, they should be immediately cleaned, first with water, then with alcohol and then with ether.

Palmer's Method of Hemoglobin Determination.—The following description of this most exact laboratory method of procedure is taken from the description of W. W. Palmer, its originator:*

"Blood is obtained in the usual manner by pricking the finger or lobe of the ear. A one per cent. solution of blood is made by drawing 0.05 c.c. into a special pipette and transferring into 5 c.c. of a 0.4 per cent. ammonia solution—accurately measured with a calibrated pipette or burette into a 12 x 120 mm. test-tube. The blood pipette is rinsed out by drawing into it two or three times the ammonia solution. Ordinary illuminating gas is bubbled rapidly through the ammonia blood solution for 30 seconds, after which, it is compared in a Duboscq colorimeter with a standard carbon monoxid hemoglobin solution set at 10. The average of at least four readings is taken. The calculation is simple, $\frac{10}{R} \times 100 =$ per cent. hemoglobin.

(*a*) "*Manner of Obtaining Blood.*—With sufficient care the usual clinical method for obtaining small amounts of blood by pricking the ear or finger is satisfactory. A free flow is essential. Any undue manipulation or squeezing of the part should be avoided because an error of 5 or 10 per cent. may be introduced by diluting the blood with tissue juice. Where there is marked anemia requiring larger amounts of blood than 0.05 c.c., or where there is difficulty in obtaining blood from the ear or finger, venous puncture should be used, coagulation being prevented with oxalate or citrate salts. It is often practical and convenient to combine the determinations of hemoglobin with other blood analyses, where venous puncture is required. If blood has been drawn by venous puncture, care must be taken that the corpuscles and serum are well mixed before filling the pipette. The blood should never be shaken violently before measuring, because it becomes filled with air bubbles. The mixture of corpuscles and serum may best be accomplished by first giving the receptacle a circular motion and finally stirring briskly with a glass rod or measuring pipette which is filled while stirring the blood.

(*b*) "*Pipette for Measuring Blood.*—The pipettes are made of millimeter glass tubing calibrated to contain 0.05 c.c. and 0.1 c.c. The pipettes are easily made in any laboratory from straight tubing, and require no blowing, the point being rounded off on an emery wheel. In this way time and expense are saved, since pipettes obtained from glass blowers require recalibration before use. It has been found that water may be used for this calibration, as pipettes which have been calibrated with mercury and water check sufficiently well. The advantage of having the pipette calibrated to contain 0.1 c.c. as well as 0.05 c.c. is obvious. In bloods with a low hemoglobin content, 0.05 c.c. may not be sufficient to give color necessary for accurate color comparison in the colorimeter. A pipette of this type, and used in the manner described, is capable of measuring 0.05 c.c. of blood with an accuracy of 0.2 per cent.

(*c*) "*Ammonia Solution.*—Ammonia solutions, containing 4 c.c. (64.8 minims) of strong ammonia in 1 liter (2.1135 pints) of water, suggested by Krogh, are used because the full color of the carbon monoxid hemoglobin develops at once.

(*d*) "*Saturation with Carbon Monoxid.*—Ordinary illuminating gas as a source of carbon monoxid has proven entirely satisfactory. It was thought that there might be substances other than carbon monoxid in the gas which might form hemoglobin compounds and interfere with the determination. Accordingly, pure carbon monoxid was prepared by heating oxalic acid with concentrated sulphuric acid and passing the gas produced through sodium hydroxid to free it from carbon dioxid. As far as could be determined on comparison of the two solutions in the colorimeter, the colors were identical. Oxyhemoglobin solutions are very unstable. Hence it is necessary, after transferring the blood to the ammonia solution, to saturate with carbon monoxid within an hour. After saturation with carbon monoxid, the solution may, on carefully stoppering and protecting from light, be placed in the ice box and the determination made at leisure. Saturation of the blood should be carried out under a hood. If the laboratory does not possess a hood, the saturation may be accomplished under a funnel, attached to a small water vacuum pump, to remove the gas.

(*e*) "*Standard Hemoglobin Solution.*—Haldane's standard of a 1 per cent. solution of a blood having an oxygen capacity of 18.5 per cent. is used. It has been shown by Haldane and Smith, Butterfield, Barcroft, and others, that the oxygen capacity of the blood depends upon its hemoglobin content. A blood of 18.5 per cent. oxygen capacity contains approximately 14 grams (216.05 grains) of hemoglobin per 100 c.c. (3.38 fluidounces). Although the blood of normal men in this country, as shown by Meyer and Butterfield, Williamson, and also as we have found by use of the method here described, contains on the average of 16.6 grams (256.138 grains) of hemoglobin, which would correspond to an oxygen capacity of about 22 per cent., it was thought best to keep Haldane's standard for the present. It is a simple matter to compute the grams of hemoglobin in any given blood from the results obtained.

---

* Journ. Biol. Chem., 1918, xxxiii, 119.

"The standard hemoglobin solution is prepared as follows: A quantity of defibrinated human or ox blood is obtained. The oxygen capacity is determined by the method of Van Slyke. The blood may also be standardized by a spectrophotometer or solutions made from hemoglobin crystals prepared in the manner described by Butterfield. We have checked several times our standard and found that the oxygen capacity method for standardization is most convenient and satisfactory. The blood is diluted with a 0.4 per cent. ammonia solution so as to make a 20 per cent. solution of a blood with an oxygen capacity of 18.5 per cent. This 20 per cent. blood solution is then saturated with carbon monoxid by bubbling through illuminating gas for 10 minutes. A drop of caprylic alcohol prevents troublesome foaming. The glass tube through which the gas is passed into the blood solution is withdrawn slowly and the bottle stoppered immediately. Rubber stoppers must not be used in connection with hemoglobin solutions. The cork should be sealed in with paraffin and the solution, protected from light, kept in the ice chest. Such a solution thus protected will keep for months. Several solutions now nearly a year old prepared in this manner have shown no deterioration. Five cubic centimeters of this 20 per cent. blood solution made up to 100 c.c. with 0.4 c.c. of ammonia solution and saturated with carbon monoxid, make the 1 per cent. standard for use in the colorimeter and may be prepared from time to time as desired. The 1 per cent. standard for a routine use may be kept in a dark glass or black painted aspirator bottle, the lower opening of which is provided with a cork, through which passes a glass tube with a ground glass cork for withdrawing small amounts of solution. A glass tube is put through the cork in the top of the bottle and extends to the bottom. Both corks should be sealed with paraffin. This glass tube is connected with an open gas fixture in order that when solution is withdrawn from the bottom, gas rather than air will enter to replace it. Solutions thus prepared may keep for several weeks; but, as a precaution, it is advisable to make fresh 1 per cent. solutions frequently, *i. e.*, every two or three weeks. It should be remembered that dilute hemoglobin solutions are less stable than concentrated solutions; and that hemoglobin solutions keep best in the cold and protected from light. The first indication of solution deterioration is a change in color from the characteristic cherry-red of carbon monoxid hemoglobin to a red with a brownish tinge, due to the formation of methemoglobin.

(*f*) "*Comparison in Colorimeters.*—The Duboscq or Kober colorimeters have proven to be by far the most accurate and satisfactory instruments for this colorimetric work. Other colorimeters, however, may be used. The difficulties encountered are those inherent in all colorimetric work, and in this connection reference to Kober's article may be made. The color of the carbon monoxid hemoglobin, because of the relatively low stimulus threshold for the eye, is admirably suited to colorimeter comparison, slight differences being easily detected. We prefer to use the daylight from a north window. Satisfactory results are, however, obtainable with artificial light when "daylight glass" is used between the source of light and the solution. Considerable experimentation with light filters has failed to improve on the accuracy with which the comparison may be made. No difficulty should be experienced in making the readings check within 0.2 of a single division on the colorimeter scale.

"Color comparisons are most accurate when the unknown hemoglobin solution reading falls between 9 and 11 on the colorimeter scale. If the reading of the unknown falls below 8 or above 12, another sample should be taken and the dilution made such that the reading will fall within these limits. This is easily accomplished by varying the amounts of blood and ammonia solution, and making the necessary correction in the colorimeter. Two cubic centimeters of solution is adequate for the Kober instrument and 5 c.c. for the Duboscq. If a Duboscq or a Kober colorimeter is not available, the Hellige instrument may be used. The one per cent. hemoglobin standard may be sealed with paraffin into the wedge and the wedge, when not in use, kept in the ice box and protected from light. Attention should be called to the fact that the scales of the Hellige colorimeter are often inaccurately placed. The standard solution must be checked against itself and the scale adjusted so as to read 100 when the color in the cup and wedge match. We have found more difficulty in obtaining accurate checks with this instrument than with the Duboscq or Kober colorimeters; but with care the error should not exceed 2 per cent. Two cubic centimeters of solution are sufficient for the Hellige cup, hence the Sahli pipette, which contains 0.02 c.c. of blood, may be used with this colorimeter. As large errors have been found in the calibration of the Sahli pipettes, it is necessary to recalibrate them before using."

The Blood-cell Count.—The differentiation of the various types of anemia requires that the number of cells contained in 1 cu. mm. of any given blood be determined directly and differentially and this is readily done with the modern apparatus. The whole process as hereafter detailed should be smartly carried out and the different steps outlined be carefully observed.

The Thoma-Zeiss hemocytometer consists of two graduated capillary pipettes, *i. e.*, the erythrocytometer and the leukocytometer for counting red and white cells respectively, and a stage carrying a ruled square millimeter which is itself divided into 400 squares of 1/20 mm. The plateau carrying the ruled surface is surrounded by a moat, the outer walls of which are 1/10 mm. higher than the ruled plateau.

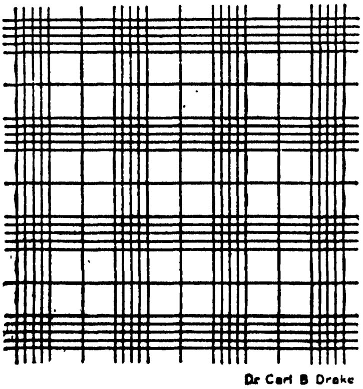


Fig. 6.—Ruling of the Gorgajew-Pappenheim Counting Chamber.

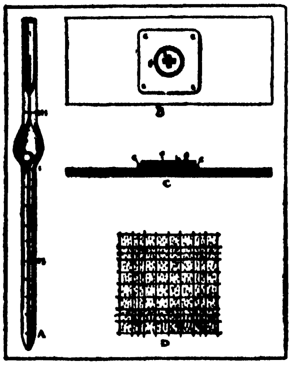


Fig. 7.—Thoma-Zeiss Blood Counter, showing Pipette, Counting Chamber and a part of the Ruled Field.

This, the older type of blood-counter, is still generally used, though the newer counting chambers are much superior.

The Red Count.—The blood is drawn into the pipette by suction or capillary attraction from the drop obtained by puncture until it reaches the point marked 1. The point is then rapidly wiped dry and the diluent quickly drawn in until it fills the bulb and reaches the mark 101.[*]

While drawing in the diluent the pipette is revolved between the finger and the thumb to set in motion the mixing bead contained in the bulb and, when filled, again thoroughly shaken and revolved for half a minute. *This mixing should be repeated each time before expelling a drop for examination.* One has then a mixture, each drop of which presents a blood dilution of 1:100.

Many prefer a 1:200 dilution readily obtained by using the mark 0.5 as the upper limit for the indrawn blood. The blood rises quickly if the pipette is perfectly clean and may exceed the proper level if not watched or checked by withdrawing the point and quickly wiping it. If the higher dilution is used, any excess is readily blown out or better *drawn down by touching the tip with filter-paper or blotter.*

---

[*] The diluent usually used is Toison's solution. Formula.—Methyl-violet 5B (0.025 gram [.3856 grain]), sodium chlorid (1 gram [15.43 grains]), sodium sulphate, (8 grams [123.46 grains]), neutral glycerin (30 c.c. [1 fluidounce]), distilled water (160 c.c. [5.38 fluidounces]).

Hayem's solution contains mercuric chlorid (0.25 gram [3.855 grains]), sodium chlorid (0.5 gram [7.715 grains]), sodium sulphate (2.5 grams [38.575 grains]), distilled water (100 c.c. [3.38 fluidounces]). Any such solution must possess two qualities,—it must prevent coagulation and be isotonic.

The next step consists in expelling the diluent occupying the capillary portion of the tube, after which a small drop of the mixture in the bulb is placed upon the central disc, the cover-glass is placed in position and the cells given time to settle.

The drop should just fill the central plateau without running over into the moat around it when the cover-glass is applied, else the process must be repeated after thoroughly cleaning and drying both the cover-glass and the counting surface.

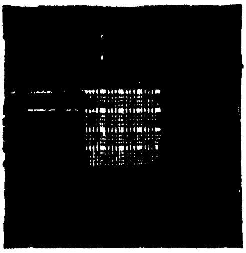


FIG. 8.—THOMA-ZEISS RULING.

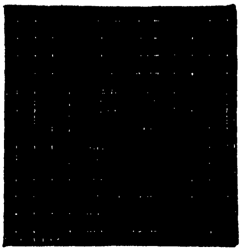


FIG. 9.—NEUBAUER'S RULING.

If the proper distribution of the drop upon the plateau has been attained, concentric color rings ("Newton's rings") should be visible when the surface of the applied cover-slip is held toward the light at, or slightly below, the level of the eyes.

The absence of these rings vitiates the count and indicates usually dust or moisture on the glass. The correct size of the drop itself must be learned by experience. It should cover the plateau without overflowing.

The specimen, when placed under a microscope carrying a Leitz No. 6 objective and No. 4 ocular or their approximate equivalents, should show a uniform distribution of blood-cells over the entire field ruled, or unruled.

Counting.—One must count now the number of red blood-cells lying within a definite known number of ruled squares, including for each square those in contact with or overlapping two of its four sides.

For thoroughly accurate painstaking work, such as would be necessary in actual research, the entire 400 squares should be counted and several drops of the mixture so treated. For clinical purposes a less number may be taken if the blood is well distributed, but several should be examined. With pencil and paper at hand an accurate record of the cell count should be jotted down as the work proceeds.

Rationale.—The number representing the total cells counted must be divided by the number of lesser squares in which they were contained. The result of this division would represent the average number of cells in each ruled square. The sides of the small squares each measure 1/20 mm. and the depth of the liquid 1/10 mm. yields a third dimension. Multiplying 1/20 x 1/20 x 1/10=1/4000 cu. mm. as the cubic content of each square used during the test.

The blood itself has been diluted 100 times. The cubic area of each smaller ruled square is 1/4000 cu. mm. We desire to record the number of erythrocytes in each cubic millimeter of the blood under examination. *We must, therefore, multiply the average number of cells per square by 4000 to get the number in 1 cu. mm. of the mixture, and this result by 100, the degree of dilution of the blood, to get the actual number of erythrocytes per cubic millimeter of the undiluted blood itself.*

This resolves itself into the following simple formula in dilutions of 1-100: *Divide the total number of red cells counted by the number of squares covered, and multiply the quotient so obtained by 400,000.* For example, one hundred squares are found to contain 1200 red cells: 1200 ÷ 100 = 12 cells per square = 12 cells in 1/4000 cu. mm. of blood diluted 100 times, and 12 x 4000 x 100 = 4,800,000 cells per cubic millimeter.

If but 40 squares were covered, 480 cells would have been counted and, by an arithmetical coincidence, all 40-square counts with a dilution of 1-100, and all counts of 80 squares with a dilution of 1-200, may quickly be determined by placing four ciphers at the right of the figures representing the total cell count, i. e. 40 squares (1-100 dilution) contain 480 cells, and 80 squares (1-200 dilution) contain 480 cells; annexing four ciphers in each instance, we have 4,800,000, the actual count per cubic millimeter.

If the entire 400 ruled squares composing the large square were counted in this case, the total cells enumerated would have been 4,800, or ten times the number of cells in our 40 squares and would represent the number of red cells in 1/10 cu. mm. of blood diluted 100 times, *i. e.* 1/1000 of the number contained in a cubic millimeter of the undiluted blood.

Hence in counting 400 squares the exact number of red cells per cubic millimeter of blood may be determined by annexing three ciphers to the number representing the total of cells enumerated in the entire large square.

If to be again used at once, air should be blown through the mixing tube by means of a hand bulb and rubber tube, not the mouth. The counting chamber should be cleaned with cold water only and should not be exposed to high degrees of heat, or, for long, even to direct sunlight, for fear of softening the cement.

THE LEUKOCYTE COUNT.—For this the large-calibered pipette is used with a diluent consisting of a 1 per cent. aqueous solution* of glacial acetic acid which leaves visible only the white cells and the nucleated reds. This pipette is graduated in tenths to a point 1 (one) for the measurement of the blood used and shows also a symbol 11 (eleven) above the bulb containing the mixture of blood and glacial acetic acid solution. When filled, the blood is ten times diluted.

The most accurate counts are made by using 0.5 rather than 1 as the basis of dilution, and even this requires a good-sized drop of blood. Furthermore, the pipette must be kept nearly horizontal at the time and after the diluent is added, else it will run out of the tube.

The diluent is added to the point 11 and the count made with the erythrocyte counting chamber, or better with Türck's chamber in which the central ruled square (*one square millimeter* [1/10 cu. mm.] containing 400 small squares) is surrounded by eight partially ruled squares of the same size. The total obtained by counting the leukocytes in the nine square millimeters (representing 3600 small squares) is multiplied by 200 (dilution 20 by 10 to get cubic millimeters) and divided by 9, assuming a dilution of 1-20 as above described.

---

* A 1 per cent. solution of glacial acetic acid is more certain in its action and a few drops of methyl violet or gentian violet stain may be added to advantage.

The actual count is based, therefore, upon the total count of white cells in any number of square millimeters, multiplied by the dilution, multiplied again by the third dimension of the cubic millimeter (10) and divided by the number of large squares (square millimeters) covered in the count.

If the ordinary counting chamber is used, the entire field of 400 ruled squares should be counted and the total number of leukocytes found multiplied by 100 if the dilution be 1-10 or by 200 if it be 1-20. The process is greatly facilitated by inserting in the tube of the ocular an eyepiece diaphragm which will cut off exactly 100 of the small squares. This may be bought, or can be made by the physician from metal or cardboard. The leukocytes in 400 small squares of the erythrocyte chamber may then be rapidly counted, together with as many additional outside diaphragm fields as are necessary to correct work.

Accurate white blood counts require patience and the counting of a large number of fields, for a slight error has a disastrous effect. Usually 2 drops of the 1-10 or 4 drops of the 1-20 dilution will enable one to count 140 to 150 cells.***

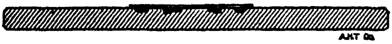


FIG. 10.—VERTICAL LONGITUDINAL SECTION OF SLIDE, WITH COVER GLASS IN POSITION, SHOWING NEW METHOD OF CONSTRUCTION.

Differential Counting.—This involves the examination of from 500 to 800 leukocytes in fixed and stained blood smears, and a determination of the exact number of each variety present. The field should be systematically and carefully gone over, and if ordinary care is observed the procedure offers no difficulty for one who is sufficiently skilled to recognize the various types of white cells and the abnormal erythrocytes which should be included in any such procedure. The process is tedious but oftentimes necessary and valuable, and necessitates, as a rule, the counting of at least two or three entire stained smears.

Important Detail.—The blood counter pipette must in every case be cleaned immediately after using: first, with water; second, with alcohol; third, with ether; and the glass bead should be absolutely free and movable after the process is completed.

MANY TYPES OF BLOOD-COUNTERS.—There are many modified forms of the "blood-counter" of the Thoma type and amongst them is one of American make and easily procurable. This is the Thoma-Levy hemocytometer and is thus described by the manufacturers:

"The Bürker type of counting chamber, of either the new or old construction, has a further advantage over the original Thoma construction—which consists of a circular ruled disc cemented on the slide in the center of a circular cell, also cemented on the slide—in that capillary attraction is used to fill the Bürker cell after the cover-glass is

---

* The ingenious self-filling and self-measuring pipette of Durham has many advantages but requires separate mixing vessels.

** In the leukemias the leukocyte count is best made with the ordinary erythrocyte counter and pipette for the dilution should be 1-100 rather than 1-10 or 1-20.

in position. This method insures a much more uniform distribution of corpuscles over the entire field and the effect of atmospheric pressure upon the depth of the solution is materially lessened. These new Thoma-Levy counting chambers of the Bürker type are now supplied with various rulings, *i. e.* Thoma, Zappert, Türck, Neubauer, Fuchs-Rosenthal, etc. The Neubauer ruling is now recommended as the most satisfactory for modern technic. The method of ruling used in the manufacture of these chambers provides a line with absolutely clean-cut edges and of distinctly increased visibility when the chamber is filled with solution for the count. This increase in visibility of the ruling greatly lessens the eye fatigue experienced in making repeated counts.

''In the old type of Bürker chamber two ruled areas are provided upon rectangular pieces of glass cemented on the main slide. These ruled rectangles were separated by a small moat to allow free passage of the diluted blood. On either side of these ruled rectangles two unruled rectangular pieces of glass were cemented which extended the entire width of the slide. These were exactly 1/10 mm. thicker than the ruled rectangles, so that when the cover-glass rested on these the required depth of solution over the ruled area was attained.''

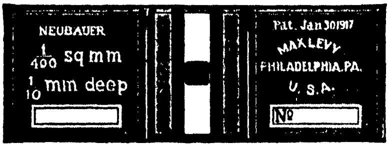


FIG. 11.—THOMA-LEVY COUNTING CHAMBER WITH ORIGINAL THOMA RULING.

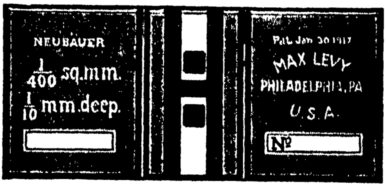


FIG. 12.—THOMA-LEVY COUNTING CHAMBER, BÜRKER DOUBLE TYPE WITH TWO NEUBAUER RULINGS.

In the Levy construction a rectangular depression is cut into the slide itself extending across the entire width. In the middle of this depression is permanently fixed a rectangular strip of glass, also extending entirely across the slide, and on this are the rulings. When the cover-glass is placed in position on the slide itself the solution over the ruled areas is of the required depth. The method of construction entirely removes the possibility of the loosening of the cell by the drying out of the balsam cement and reduces the possibility of the loosening of the ruled counting surface.

In the Bürker-Neubauer counting chambers the rectangular glass in the center of the cell is divided by a central moat, each half being provided with a Neubauer ruling, so that both red and white counts may be made at the same time without the necessity of cleaning and refilling the counting chamber.

The Neubauer modification of the original Thoma ruling is probably the most satisfactory of all. In it the central square millimeter is exactly the same as in the original Thoma ruling. Surrounding this there are 8 additional square millimeters, each subdivided into 16 smaller squares, and these are of extreme value by reason of the greater accuracy and convenience which they afford in counting the white blood corpuscles.

The actual technic for using the Bürker chamber is extremely simple and may be briefly summarized as follows:

1. The ruled areas and slide are carefully cleaned and made absolutely free from dust.
2. The cover-glass is applied and Newton's rings* must be obtained as evidence of the approximation of the two surfaces.

---

* The Newton's interference rings are not readily obtainable in the Levy construction as in the older type because of the mat or ground surface of the slide upon which the cover-glass rests, but because of this mat surface accurate approximation of the surface of the cover-glass and slide is readily obtained.

The original Bürker instrument and Gorgajew-Pappenheim modification of it carry clamps which aid in obtaining and maintaining accurate contact (*Author*).

3. The tip of the projecting ruled rectangle is quickly touched with the point of the filled red or white blood pipette, permitting the diluted blood to flow under the cover-glass to just the extent sufficient to cover completely the ruled rectangle but not flow over into the moat on either side. No bubbles should form in this process.

4. After allowing three minutes for settling, the evenness of distribution is determined either by low-power examination with the microscope or by placing the counter upon the stage of the microscope, which is illuminated by a mirror with the diaphragm open as wide as possible. If now the counting surface is viewed obliquely with the unaided eye, any irregularity in the distribution of the cells is easily recognized by variations in the density of the blood film. If such irregularities are observed, the cover-glass should be removed, the chamber carefully cleaned, and the procedure repeated.

Fig. 13.—Mixing Pipette for Red Corpuscles.

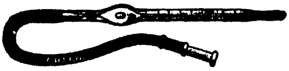


Fig. 14.—Mixing Pipette for White Corpuscles.

Fig. 15.—Hemacytometer (the Thoma-Metz).

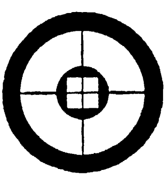


Fig. 16.—Eye-piece ruling of Thoma-Metz.

The Thoma-Metz Hemocytometer.—The counting plate is mounted in the plane of the ocular diaphragm of eyepiece No. 11. The Leitz objective No. 6 is used in connection with it. The dilution of the blood is carried out with the aid of two Thoma pipettes of regular type, following the known method.

The large square in the center of the counting plate is divided into four smaller squares and serves for the counting of the **red blood corpuscles.** The large square is surrounded by a **circle** which is divided also into four parts of equal area, serving for the counting of **white blood corpuscles.** The regular chamber of 0.1 mm. depth is used for the counting by this method.

(1) *Directions for the Counting in a Solution of 1 Cu. Mm.*—(*A*) *For Red Blood Corpuscles.*—The dimensions of the large square of the

counting plates are so calculated that one side of same covers 0.1 mm. of the object. The area, therefore, is equal to 0.1 x 0.1 = 0.01 sq. mm., and the cubic contents of that area of the object as covered by the entire square is equal to 0.01 x 0.1 = 0.001 cu. mm. The number of red corpuscles in the solution—diluted 1 : 100—amounts, therefore, to 100 x 1000 = 100,000 times the corpuscles found in the square counted. For example, 52 red corpuscles found in the square shows 52 x 100,000 = 5,200,000 red corpuscles in 1 cu. mm. of solution. In order to achieve a reliable average count it is advisable to move the slide and count in various zones of the solution.

(*B*) *For White Blood Corpuscles.*—The circle established for the counting of white corpuscles covers ten times as much area as does the square for the counting of red corpuscles. This circle, therefore, covers an area of 10 x 0.01 = 0.1 sq. mm. of the counting chamber of a depth of 0.1 mm., and the cubic contents amount to 0.1 x 0.1 = 0.01 cu. mm. The actual number of white corpuscles as contained in the solution—diluted 1 : 10—will, therefore, amount to 10 x 100 = 1000 times the number as found in the circle. For example, 8 white blood corpuscles found in the circle show 8 x 1000 = 8000 white corpuscles in 1 cu. mm. of solution. In order to achieve a reliable average count, it is advisable to move the slide and count in various zones of the solution.

The factor, 100 x 1000 for red blood corpuscles, is engraved in **red**, and the factor, 10 x 100 for white corpuscles, is engraved in **white** on the counting slide.

(2) *Advantages.*—The counting plate is produced in a photographic way and can be focused sharply for every eye by means of the adjustable eye lens, and therefore, the ruling appears in sharp lines in the counting field.

For the counting of red as well as of white blood corpuscles separate fields are used. These fields are, in their area, so adjusted that a unit for multiplication is established. *This factor allows quick counting.*

The apparatus is adjusted for an optical equipment of objective No. 6 (4 mm. focal length) and ocular No. 11 (5X), as these are the lenses mostly used for blood-counting work. Small variations, as far as lenses of other makes are concerned, can be overcome through the adjustment of the tube length. On the bottom of the slide, a square is drawn and the proper optical relation is established when this square covers the large square of the counting plate. (The author has had no experience with the instrument and has been unable to secure one for test purposes.)

Oliver's Hemocytometer.—This ingenious instrument, save in the severer types of anemia and in leukemia where the excess of leukocytes vitiates any optical method, is fairly accurate in skilled hands.

(1) *Method.*—A small amount of Hayem's solution is placed in the glass tube and into it is stirred the blood taken up by the capillary pipette. In a dark room it is then diluted gradually with the Hayem's mixture until a bright horizontal line becomes visible as the observer looks through the mixture at a candle flame beyond. Each point on the scale represents 50,000 red cells.

(2) *Precautions.*—(*a*) One looks at the edge of the tube, not at its flat face. (*b*) The pipette should be thoroughly clean before being used. (*c*) The tube should be inverted to secure proper admixture each time that the diluent is added. (*d*) An imperfect marginal line forecasts the appearance of the complete transverse line and warns one to go slowly with

the dilution. (*e*) A small Christmas candle should be used in a dark room. (*f*) The tube should be close to the eye and the observer fully 10 feet from the candle.

The procedure is seldom employed at the present time. It has too limited a range and the personal equation is too great a factor.

The Hematocrit (Hedin-Daland).—This consists of a graduated capillary tube, each degree of which represents 100,000 erythrocytes. The tube is filled with blood and placed (with a similar tube opposite) in the centrifuge which should be revolved at high speed for at least two minutes, when the red column will represent the erythrocytes present as indicated by the scale. The tube when filled by suction is dried and closed at its other end by the vaseline-coated finger which is kept in place while the rubber suction tube is withdrawn. The results obtained are rapid but only approximate when used in the severer types of anemia. As pointed out by Capps, it affords a means of obtaining information relating to cell volume.

It is a simple matter to calculate the normal height of the red blood-cell column in the hematocrit tube as compared with the height of the total blood column. This is usually 50 on the scale tube and this figure is reckoned as 100 per cent. normal.

The figure so obtained is divided by the figure representing, in percentage, the number of red cells per cubic millimeter counted in the blood of the same individual, as compared with the normal, 5,000,000 cells per cubic millimeter. The quotient is the red cell *volume index* and parallels in a considerable degree the *color index* heretofore described, both as regards its variations and their clinical significance.

The normal red cells *volume index* varies as follows: In primary pernicious anemia it is high; in secondary anemias, reduced; in chlorosis, distinctly low. *These variations, if marked, are usually obvious to the trained observer in an examination of the simple well-made blood smear.* The method may find its wider usefulness in the detection and measurement of blood changes other than those of anemia.

LEUKOCYTOSIS AND LYMPHOCYTOSIS

As ordinarily applied, the term leukocytosis covers an increase of the polymorphonuclear neutrophilic cells both relative and absolute. Lymphocytosis may be either relative or absolute, the former occurring without any necessary increase in the total white cell count, the latter covering both an increase in percentage and in the total lymphocytes. As a matter of fact the latter is usually to be interpreted as a lymphatic leukemia.

Differentiation of Leukocytosis from Leukemia.—It is not the number of white cells present in a specific amount of a given specimen of blood which differentiates leukocytosis, a mere transitory phenomenon, from leukemia, a peculiarly intractable and fatal chronic disease. The differentiation depends upon the type of cell which dominates the microscopic picture or the blood findings as a whole combined with other signs and symptoms of known character and association. With rare exceptions leukocytosis means the polymorphonuclear increase alone, or, more rarely, a general increase of leukocytes of the normal types.

Average Normal Leukocyte Count.—The leukocyte count normally may vary from 6,500 to 10,000 cells to the cubic millimeter of peripheral blood, the average being about 7,500.

Physiologic Leukocytosis.—There are several forms of physiologic leukocytosis but the only one of sufficient importance to merit particular attention is that which accompanies digestion, reaching its maximum within from two to four hours after a meal and being more marked if this is rich in proteids. Such a physiologic increase in the count usually represents polymorphonuclear forms but in some instances shows an increase of all the normal types of white cells.

It is worth remembering that in nursing infants and diabetics such a leukocytosis is particularly marked and that even in the ordinary adult the count may be increased 33 1/3 per cent.

Preagonal Leukocytosis.—Immediately before death high white blood counts may be observed, reaching or exceeding in some instances 30,000 cells per cubic millimeter. The writer can verify the statement of Cabot that in certain cases of pernicious anemia this may assume the form of so decided a lymphocyte increase as to closely simulate lymphatic leukemia. In most instances, however, it is a polymorphonuclear increase, to be attributed probably to the stasis resulting from a failing circulation and also to a profound toxemia which acts as an irritant upon the blood-forming tissues. It may be added that in these cases the primary increase is usually lymphocytic, the polymorphonuclear increase coming later.

The Leukocytosis of Pregnancy.—It is important that one should remember that both in the later months of pregnancy in primiparæ and during the first week following delivery, a moderate leukocytosis is the rule. Such a leukocytosis is ordinarily polymorphonuclear in type.

The Leukocyte Count in the New Born.—In newly born infants the white count during the first two days of life reaches ordinarily 18,000 or 20,000 and during the first year it may remain at between 10,000 to 15,000 leukocytes per cubic millimeter.

It should be remembered in this connection that in infants the lymphocytes and transitional cells may constitute 55 or 60 per cent. of the total white cells present, a gradual reduction to normal ratios bringing the figures down to the norm at the age of four or five years. In other words, the increased percentage of lymphocytes occurring in connection with an increase in the total white cell counts in infants ordinarily has no clinical significance.

The Leukocytosis of Disease.—So many diseases show clinically a more or less marked increase in white blood-cells at some stage of their development or progress as to make it hardly worth while to enumerate the ailments in detail. Indeed, it is more useful ordinarily to remember the exception, or better still, the diseases in which the number of white cells per cubic millimeter of the blood is diminished (leukopenia).

Most of the acute infections attended by an inflammatory process, and particularly such as involve the serous membranes, and any suppurative process attended by toxemia, would be expected to produce a leukocytosis. It is true, nevertheless, that under certain conditions this phenomenon is lacking (*a*) because the extent of the inflammation or of the toxemia may be too slight to excite a reactive change in the blood-forming tissues, (*b*) because the toxin overwhelms the organisms through excessive virulence and inhibits leukocytic reaction, or (*c*) because the person involved is too much enfeebled and nonresistant to show a leukocytosis.

Lobar pneumonia presents a frank and often extreme leukocytosis. Typhoid fever, on the other hand, a disease attended by most profound exhaustion, is associated with a leukopenia save in the presence of some complication of an inflammatory type.

If one considers the nature of these two diseases as ordinarily manifested he can understand why there should be this wide divergence. Lobar pneumonia is frank and sudden in its onset, rapid in its development and sthenic in type; whereas typhoid fever is gradual in onset, insidious in development and directly prostrating and asthenic in its nature. One can understand easily that a case of frank lobar pneumonia, as determined by the physical signs and associated symptoms, which shows a leukopenia, offers an extremely hopeless prognosis, and that a case of genuine typhoid fever which develops a leukocytosis must be assumed to be carrying some extraordinary complication.

Acute suppurative appendicitis again and again illustrates the significance and importance of a leukopenia, for ordinarily it yields a well-defined leukocytosis representing presumably a good defensive mechanism on the part of the patient, yet we find most serious cases in which there is no leukocytosis and even a reduction below the normal number because of an overwhelming toxemia or defective defensive mechanism.

It should be remembered that a leukocytosis may be present in malignant disease, especially if there be a rapidly growing tumor or tumors in the kidney, lungs or liver, and in the author's experience a leukocytosis is especially common in this connection in metastatic hepatic invasion from gastric carcinoma. In uremia, cholemia, ptomain poisoning and gas poisoning the increase of white cells may be marked; so also in cases of acute delirium, convulsions, immediately after surgical operations, or indeed following profound general anesthesia. It is said that in actual suppuration or gangrene and consequent septic absorption, the polymorphonuclear percentage of an increased count will exceed 85 per cent. It is also asserted that the total numerical increase of leukocytes in a given case may be regarded as measuring the resistance of the organism, whereas the percentage increase of polymorphonuclears represents the degree of toxemia.

Definition of Leukopenia.—To establish a standard it is customary to assume that any leukocyte count running below 5,000 cells per cubic millimeter represents a leukopenia. It must be understood, however, that a reduction in the white cell count is to be anticipated in the profound anemias of the pernicious type especially, or in any ailment associated with chronic extreme malnutrition or starvation. In other words, the chief importance of leukopenia as a symptom rests in its appearance in diseases of the infectious and toxemic type.

CERTAIN DISEASES ASSOCIATED WITH LEUKOPENIA.—Some of the chief ailments showing a diminution in the white count are typhoid fever, paratyphoid fever, influenza, Malta fever, malaria, measles and rötheln, leprosy, trypanosomiasis, and, in the absence of septic symptoms, tuberculosis. It is sometimes observed in chlorosis, chronic infantile gastroenteritis and as a result of the administration of atropin, ergot, camphoric acid, agaricin, picrotoxin, sulphonal and tannic acid.

Lymphocytosis.—Either the large, small, or the transitional mononuclear forms may predominate in any case of lymphocytosis and the condition is of pathologic significance when occurring in children above the age of five or in adults. Such an increase in the ratio of the mononuclear cells apart from lymphatic leukemia, in which there is both a relative and absolute increase, is associated usually with profound malnutrition and therefore is especially likely to be encountered to a marked degree in the terminal stages of the asthenic and exhausting type. We would expect to find this symptom in malaria of the severer types, typhoid fever, Malta fever, diphtheria, tuberculosis and trypanosomiasis, and we also find it in scarlet fever, measles and other ailments markedly involving the lymphatic glands. It follows the administration of thyroid substance, quinin, pilocarpin, occurs perhaps combined with eosinophilia in syphilis, and is present with peculiar frequency in infections associated with marked splenic enlargement and in the invasion of lymph channels by malignant growths.

Eosinophilia.—The presence of this condition is determined by a differential blood-count establishing the proportion of eosinophil cells to the total leukocyte count, the latter multiplied by the former giving the total number of eosinophils per cubic millimeter of a given blood.

Eosinophilia is present in so large a number of diseases as to greatly lessen its clinical significance and importance, but its constancy as a symptom in trichiniasis, hydatid disease, and cases of invasion by the more important intestinal parasites is so marked as to make it of some clinical value.

It is constantly present in spasmodic asthma, may be combined with lymphocytosis in syphilis, as has been stated previously, and in scarlet fever may make its appearance after an antecedent leukopenia which gives place to a marked leukocytosis with increase in the eosinophil cells.

Attempts have been made to create a disease group in relation to which an eosinophilia should be considered as pathognomonic, but this effort of foreign observers has not met successfully the test of clinical experience.

Blood-platelets.—The function of the blood-platelets, as at present understood, is the release of prothrombin and thromboplastin under conditions of normal degeneration.

In any hemolytic process the blood-platelets and megakaryocytes from which they originate are affected adversely. But it would appear also that a reduction in their numbers may occur under other conditions such as do not affect the other constituents of the blood.

Their numbers are diminished in nearly all infectious diseases, purpura, leukemia and hemophilia, as well as in pernicious anemia, and in general a diminution is observed in states associated with malnutrition and marked cachexia.

They are increased in scarlet fever, in most cases of chlorosis, in septic poisoning, and after hemorrhage.

Counting the Blood-plates.—INDIRECT METHOD.—This requires a diluting fluid * through a drop of which placed upon the finger the puncture is made. After mixing, a differential count is made to determine the ratio of plates to erythrocytes. It is then necessary to count only the erythrocytes by means of a counting chamber to know the number of plates present in the given specimen.

DIRECT METHOD.—The direct method of Wright and Kinnicutt is preferable. One employs as diluting fluid solutions of *brilliant cresyl-blue* (1:300, aqueous) and potassium cyanid (1:1400, aqueous). The solutions are mixed just before use in the proportion of two parts of the former to three parts of the latter. The original solutions must be freshly prepared, or refrigerated if kept as stock solutions. The blood-platelets appear clearly defined as oval, round, or somewhat elongated bodies, stained lilac and sharply contrasted with the leukocytes, which show a deep blue nucleus and light blue protoplasm. The red cells are decolorized. The size of the platelets is variable, being larger when few are present, smaller when occurring in increased numbers, but they average about 3 microns in diameter. Normally their numbers vary from 150,000 to 300,000 per cubic millimeter, and *the count is made exactly as in the case of the erythrocytes.*

---

* Aqueous solution of sodium chlorid 1 per cent. and potassium bichromate 5 per cent. (Determann).

Determination of Hemolytic Resistance.—If blood is added to water it immediately *"lakes," i. e.* gives up the hemoglobin of its erythrocytes to the liquid. If the osmotic pressure is equalized by the addition of some suitable substance such as sodium chlorid (0.9 per cent.) the solution becomes isotonic and no "laking" occurs. By using properly graduated solutions of sodium chlorid or other substances the resistance of any given blood to hemolysis may be determined. The same process is applied in determining the proper donor of blood for transfusion, for both donor and patient must belong to the same group with respect to cell resistance whether to isohemolysins or isoagglutinins.

Total Blood Volume.—It is wholly probable that the ingenious and relatively simple procedure of Keith, Rowntree and Geraghty will supplant the methods of Haldane and Smith, Morawitz, Zuntz and Plesch, Abderhalden and Smith, and von Behring. The principal feature of this latest procedure is the introduction into the blood of a rapidly diffusible, slowly absorbable dye, known as "vital red" (disodium-disulphonaphtholazotetramethyl triphenyl methane), and colorimetric comparison with a properly standardized mixture of the dye and the unstained plasma of the patient. Its slow absorption and elimination and relative nontoxicity (3 c.c. [48.6 minims] per kilo [2.71 lbs.] of body weight being wholly without poisonous effects) insure the possibility of sufficient time retention to guarantee thorough mixing with the plasma. without appreciable loss of the dye, unless to some slight extent through fixation by the tissues.

The results obtained agree more closely with the older ideas than with the modern views as to the relation of total blood volume to body weight. Keith and his co-workers find that the average blood volume is 85 c.c. (2.83 fluidounces) per kilo (2.71 lbs.) of body weight, equal to one-eleventh of the body weight, and varying between that figure and one-thirteenth. As regards the partition of the blood components, 57 per cent. was found to represent plasma, and 43 per cent. erythrocytes and leukocytes. The plasma content as determined by the hematocrit varies from 42 to 56 c.c. (1.40 to 1.86 fluidounces) per kilo (2.71 lbs.) of body weight.

One of the interesting results reported bears upon blood volume in arterial hypertension, or hypotension. In the chronic hypertension of renal cases, it was found normal or even decidedly reduced. In obesity the blood (and plasma) volume is reduced; in anemia it is often increased as to total plasma.

The actual technic while relatively simple is too extended to receive detailed description in a work of this type and too time-consuming and exacting in its demands to make it of general availability to the practitioner, in the comparatively infrequent instances in which its employment might be of especial clinical interest.[*]

Coagulation Time.—It is sometimes important to estimate the coagulation period in hemophilia, purpura and in "obstruction of the biliary tract with or without jaundice" (Cabot), as in these conditions clot formation may be greatly retarded.

For accurate work the method and instrument of Russell and Brodie as modified by Boggs may be used; or for rough determinations, in the absence of better appliances, a simpler method described below may be used. In the former coagulation should occur within from three to six minutes; by the simpler method, in from two and one-half to five minutes. The latter merely involves the placing of several drops of the suspected blood upon slightly warmed microscope slides which are tilted upward at varying intervals, the elapsed time representing the coagulation period. Another rough but useful method consists in placing the drop of blood upon a *perfectly clean glass slide* and passing a needle through it every twenty or thirty seconds until the needle drags the clot.

The Boggs coagulometer consists of (*a*) a round glass-bottomed "moist chamber"; (*b*) a cover fitting into and closing the chamber and carrying in the center a cone of glass the truncate apex of which lies within the "moist chamber"; (*c*) a capillary tube opening into the side of the chamber through which a jet of air can be pumped with a hand bulb so as to impinge upon the drop of blood taken upon the tip of the glass cone for examination; (*d*) a small opening in the upper surface of the cover of the chamber, which serves as an air outlet.

PROCEDURE.—The lobe of the ear is punctured and the time of appearance of the blood accurately noted. The tip of the glass cone receives a blood drop, the cell is at once covered, the chamber is placed upon the stage of a microscope, and at intervals of 30 seconds a soft current of air is played upon the blood drop. Four stages of movement are seen to ensue as affecting the blood corpuscles: (1) independent; (2) clumped; and (3) mere "radial" mass response to the air current, denoting complete coagulation.

BIBLIOGRAPHY

Introductory Section

ABEL, J. J. Science, N. Y. and Lancaster, Pa., 1915, xliii, 135 and 165.
ADDIS, T. Arch. Int. Med., 1915, xv, 413.
ARNETH, J. Die neutrophilen weissen Blütkröperchen bei Infectionskrankheiten, Jena, 1904.
ASHBY, W. Jour. Exper. Med., 1919, xxix, 267.
BADERTSCHER, J. A. Amer. Jour. Anat., 1913-14, xv, 69.
BANG, I. Biochem. Ztschr., Berlin, 1913, xlix, 19-39.
BARCROFT, J. Ergebn. d. Physiol. (Asher u. Spiro), Weisbaden, 1908, vii, 699. The respiratory function of the blood, Cambridge University Press, 1914.
BARKER, L. F. International Clinics, Phil., 1910, 20 Series, iv, 20-38.
BARRATT, J. O. W., and YORKE, W. Brit. Med. Jour., 1914, i, 235.
BARTLETT, W. B. Boston Med. and Surg. Jour., 1907, clvi, 629.
BAYNE-JONES, S. Amer. Jour. Physiol., 1912-13, xxx, 74-79.
BENDA, C. Verhandl. d. phys. Ges. zu Berlin, 1896-97.
BERT, P. La Pression barométrique, Paris, 1898.

---

[*] Reference to the extended original article is necessary. Keith, Rowntree and Geraghty: *Arch. Int. Med.*, Oct. 15, 1915, xvi, No. 4, pp. 547-576.

Bezancon, F., and Labbe, M. Traité d'hématologie, Paris, 1904.

Bickel, A., et Tasawa, H. Charité Ann., Berlin, 1913, xxxvii, 248-251.

Bigland, A. D. Quar. Jour. Med., 1913-14, vii, 369.

Blumenthal, R. Travaux Lab. Phys. Inst. Solway, 1904, vi, 219.

Blumenthal, R., und Morawitz, P. Deut. Arch. f. klin. Med., 1907-08, xcii, 25.

Bohr, C. Handb. d. Physiol. d. Mensch. (Nagel), Braunschweig, 1909, i. 54-222.

Bordet, J. The Harben lectures, 1913, iii. The coagulation of the blood. Jour. State Med., London, 1913, xxi, 577.

Bordet, J., and Gengou, O. Ann. de l'Inst. Pasteur., Paris, 1901, xv, 129-144.

Boycott, A. E., and Douglas, C. G. Jour. Path. and Bact., 1908-09, xiii, 256.

Boyd, J. D. Jour. Lab. and Clin. Med., 1919, iv. 495.

Bramwell, B. Anemia and some of the diseases of the blood-forming organs and ductless glands. Edinburgh, 1899.

Bredichin, J. Central f. d. med. Wissensch., 1867, v, 563.

Brinckerhoff, W. R., and Tyzzer, E. E. Jour. Med. Research, 1902, iii, 449, n. s. II, p. 191.

Brown, T. R. Jour. Exper. Med., 1898, iii, 314.

Bruce, D. Proc. Roy. Soc., 1894, lv, 295.

Buchanan, R. J. M. The blood in health and disease. London, 1909, H. Frowde.

Bull, C. G. Jour. Exper. Med., 1915, xxii, 475.

Bunting, C. H. Bull. Johns Hopkins Hosp., 1911, xxii, 114, and 369; and 1914, xxv, 173 and 177. Jour. Exp. Med., 1906, viii, 625. Jour. Exp. Med., 1909, xi, 541. Bull. Johns Hopkins Hosp., 1905, xvi, 222.

Burrows, F. G. Amer. Jour. Med. Sc., 1899, cxvii, 503.

Butterfield, E. E. Ztschr. f. physiol. Chem., 1909, lxii, 173.

Butler, G. G. Quart. Jour. Med., 1912-13, vi, 145.

Cabot, R. C. A guide to the clinical examination of the blood for diagnostic purposes. 5th ed., N. Y., 1904, W. Wood & Co. Jour. Med. Research, 1903, iv, 15. Vermont Med. Monthly, Burlington, 1910, xvi, 1-4.

Cadwalader, W. B. Bull. Ayer Clin. Lab., Philadelphia, 1905, No. 2, p. 29.

Camac, C. N. B. Clinical examination of the blood. Ref. Handb. Med. Sc., 3 Ed., 1913, ii, 158.

Carnot, P. Compt. rend. Soc. biol. de Paris, 1906, lxi, 344.

Carstanjen, M. Jahrb. f. Kinderheilkunde, 1900, 3 F., II, 215.

Chamberlain. W. P. and Vedder, E. B. Philippine Jour. Sc., 1911, vi, 405.

Champy, C. Soc. d'étud. scient. et méd., Paris, 1913, 218.

Ciaccio, C. Pathologica, Geneva, 1911, iii, 13.

Clowes, G. H. A., and West, F. Proc. Soc. Exper. Bio. and Med. N. Y., 1913-14, xi, 6-8.

Cowdry, E. V. Carnegie Institution of Washington, 1918, Pub. No. 271, p. 39.

Dallwig, H. C., Kolls, A. C., and Loevenhart, A. S. Amer. Jour. Physiol., 1915, xxxix, 77.

Danilewsky, B. Arch. f. d. ges. Physiol., 1895, lxi, 264.

Davis, B. F., and Carlson, A. J. Amer. Jour. Physiol., 1909, xxv, 173.

Deetjen, H. Zeit. f. physiol. Chem., 1909, lxiii, 1.

Dickson, W. E. C. The bone marrow, 1908.

von Domarus, A. Taschenbuch der klin. Hämatologie, Leipzig, 1912, G. Thieme.

Dominici, H. In Manual d'Histologie Pathologique (Cornil, V., et Ranvier, L.), Paris, 1902, Vol. II, 586.

Douglas, C. G., Haldane, Henderson, and Schneider. Trans. Royal Soc., 1913, B., cciii, 185.

Downs, A. W., and Eddy, N. B. Amer. Jour. Physiol. 1917-18, xlv, 294; 1918, xlvi, 209; and 1918-19, xlvii, 399.

Draper, G. Bull. Ayer Clin. Lab., Phila., 1910, No. 6, 14.

Drinker, C. K. and K. R. Amer. Jour. Physiol., 1916, xl, 514. Jour. Exper. Med., 1918, xxvii, 249 and 383.

Drinker, C. K., and Brittingham, H. H. Arch. Int. Med., 1919, xxiii, 133.

Drysdale, J. H. Clinical examination of the blood and its significance. Allbutt & Rolleston's System of Medicine, London, 1910, Vol. I, p. 640-701.

Duke, W. W. Arch. Int. Med., 1913, xi, 100.

Emerson, C. P. The blood. In Clinical Diagnosis, 1913, 561, Phila. and London.

Emmel, V. E. Amer. Jour. Anat., 1914, xvi, 127.

Erben, F. Zeits. f. Heilk. (Int. Med. Abt.), 1903, xxiv, 70.

Erdmann, R. Proc. Soc. Exper. Biol. & Med., 1916-17, xiv, 109.

Ehrlich, P. Nothnagel's System of Medicine, Amer. Ed., 1905, Vol. IX, 85.

Evans, F. A. Arch. Int. Med., 1916, xvii, 1.

Evans, H. M. Anat. Rec., 1914, viii, 98 and 99. Science, 1914, n. s. xxxix, 843.

Evans, H. M., Bowman, F. B., and Winternitz, M. C. Jour. Exper. Med., 1914, xix, 283.

Evans, H. M., and Schulemann, W. Science, 1914, n. s. xxxix, 443; Deutsch. med.. Wchnschr., 1914, 1508.

Ewing, J. Clinical pathology of the blood. 1901, 84, and 132, Lea & Febinger, Phila. N. Y. Med. Jour., 1895, lxi, 257.

Ferrata und Negreiros-Rinaldi. Fol. Med., 1915, i, 418.

Flemming, W. Arch. f. mikr. Anat., 1884, xxiv, 50.

Folin, O. Einige f. Blut- und Harnanalyse best. Schnellmethoden. Handb. d. Biochem Arbeitsm. (Abderhalden), 1913, vii, 715.

Fonio, A. Cor.-Bl. f. schweiz. Aerzte, 1915, xlv, 1505.

Gaule, J. Arch. f. d. ges. Physiol., 1902, xc, 119.

Giffin, H. Z., Sanford, A. H., and Szlapka, T. J. Amer. Jour. Med. Sc., 1918, clv, 562.

Gilbert et Weinberg. Traité du sang, Paris, 1913.

Goldscheider, A., und Jacob, P. Zeit. f. klin. Med., 1894, xxv, 373.

Goodall, A., Gulland. G. L., and Paton, D. N. Jour. Physiol., 1904, xxx, 1.

Goodall, A., and Paton, D. N. Jour. Physiol., 1905, xxxiii, 20.

Graham, G. S. Jour. Med. Research, 1916, xxx, 231.

Grawitz, E. Klinische Pathologie des Blutes. Leipzig, 1911, G. Thieme, p. 1011.

Greene, C. L. Medical Diagnosis, 4th Ed., p. 110, P. Blakiston's Son & Co., Phila., Pa.

Gulland, G. L., and Goodall, A. The blood: a guide to its examination and to the diagnosis and treatment of its diseases. Edinburgh & London, 1912, Green & Sons.

Gundobin, N. Jahrb. f. Kinderheilkunde, 1893, xxxv, 187.

Haldane, J. S., Organism and environment as illustrated by the physiology of breathing. New Haven, 1917.

Haldane. J., and Smith, J. L. Jour. Physiol., 1899-1900, xxv, 331.

Hall, W. S., and Eubank, M.D. Jour. Exper. Med., N. Y., 1896, i, 656.

Hansmann, G. H., and Howard, C. P. Jour. Am. Med. Assn., 1919, lxxiii, 1262.

Harrop, G. A., Jr. Arch. Int. Med., 1919, xxiii, 745.

Harvey, W. H. Jour. Physiol., 1906, xxxv, 115.

Harvey, W. F., and Acton, H. W. Indian J. M. Research, Calcutta, 1914-15, ii, 721-732.

Hawes, J. B., 2nd. Boston Med. and Surg. Jour., 1909, clxi, 493.

Hawk, P. B. Amer. Jour. Physiol., 1903-04, x, 384.

Hess, A. F. Jour. Exper. Med., Lancaster, Pa., 1915, xxi, 338.

Hill, E., Morton, J. J., and Witherbee, W. D. Jour. Exper. Med., 1919, xxix, 89.

Hirschfeld, H. Berl. klin. Wchnschr., 1901, xxxviii, 1019.

Hirschfeld und Klinger. Biochem. Ztsch., Berlin, 1915, lxviii, 163.

Hoeber, R. In Handb. d. Biochem. (Oppenheimer), Jena, 1909, ii, 1-38.

Hooper, C. W., and Whipple, G. H. Jour. Exper. Med., 1916, xxiii, 137. Amer. Jour. Physiol., 1916, xl, 332, and 349; xlii, 256, 264, 280, and 544; 1917, xliii, 258, 275, and 290.

Howell, W. H. Amer. Jour. Physiol., Boston, 1911-12, xxix, 187-209. Therapeut. Gaz. Detroit, 1912, 3rd Series, xxviii, 95. Amer. Jour. Physiol., 1912-13, xxxi, 1-21. Amer. Jour. Physiol., 1910, xxvi, 453-473. Amer. Jour. Physiol., Baltimore, 1914-15, xxxv, 1-7. Jour. Morphol., 1890, iv, 57, and 117.

Hoyer, H. Centralb. f. d. med. Wissensch., 1869, pp. 244 and 257.

Hunter, W. Abstr. Proc. Royal Soc., Edinburgh, 1884-86, xiii, 849.

Hunter, W. K. Recent advances in hæmatology. London, 1911, H. Kimpton.

Hutchison, R. Lancet, 1904, i, 1253.

Itami, S. Arch. f. exper. Path. u. Pharm., 1908-09, lx, 76.

Japha, A. In Handb. d. Kinderh., 2nd ed. (Pfaundler u. Schlossmann), Leipzig, 1910, ii, 1-49.

Jolly, J. Arch. Anat. Microsc., 1906-07, ix, 133.

Jordan, H. E. Amer. Jour. Anat., 1918, xxiv, 225.

Juspa, V., and Krause, L. Folia Hæmat., 1913-14, xvii, 429.

Källmark, F. Folia Hæmat., 1911, xi, 411.

Kemp, G. T. Amer. Jour. Physiol., 1903-04, x, xxxiv.

Kepinow, L. Biochem. Ztschr., 1910-11, xxx, 160.

Kerr, W. J., Hurwitz, S. H., and Whipple, G. H. Amer. Jour. Physiol., 1918, xlvii, 356, 370, 379.

Kite, G. L. Jour. Infect. Dis., 1914, xv, 318; and 1915, xvi, 109.

Klein, S. Die Myelogonie als Stammzelle der Knochenmarkszellen im Blute und in den blutbildenden Organen und ihre Bedeutung unter normalen und pathologischen Verhältnissen. Berlin, 1914, J. Springer.

Kober, P. A. Jour. Biol. Chem., 1917, xxix, 155.

Kölliker, A. Ztsch. f. rationelle Med., 1846, iv, 112. Handbuch der Gewebelehre, Leipzig, 1889, i, 297.

Krumbhaar, E. B. Ann. Surg., 1917, lxvi, 133.

Krumbhaar, E. B., and Musser, J. H., Jr. Jour. Exp. Med., 1914, xx, 108.

Kyes, P. Internat. Monatschr. f. Anat. u. Physiol., Leipzig, 1914-15, xxxi, 543. Anat. Record, Philadelphia, 1915, ix, 97.

Lamson, P. D. Jour. Pharm. and Exper. Therap., 1915, vii, 169.

Langer, K. Denkschriften der Kaiserlichen Akademie der Wissenschaften, 1876, xxxvi, 1.

Larrabee, R. C., Tileston, W., and Emerson, W. R. P. Boston Med. and Surg. Jour., 1903. cxlviii. 199.

Lee, R. I., and Robertson, O. H. Jour. Med. Research, 1915-16, xxviii, 323.

Lee, R. I., and Vincent. B. Arch. Int. Med., 1914, xiii. 398.

Letsche, E. In Handb. d. Biochem. Arbeitsm. (Abderhalden), 1911. v, 139.

Limbeck, R. R. Grundriss der klin. Path. des Blutes, Jena. 1896. G. Fischer.

Lobenstine, R. W. Amer. Jour. Med. Sc., 1904, cxxviii, 281.

Longcope, W. T. Bull. Ayer Clin. Lab., Philadelphia, 1907, iv. 6.

Longcope, W. T., and Donhauser, J. L. Jour. Exper. Med., 1908, x, 618.

Löwit, M. Studien z. Physiol. u. Pathol. d. Blutes, v. d. Lymphe, 1892.

MacCallum, W. G. A textbook of pathology, 1918, 735.

McJunkin, F. A. Arch-Int. Med., 1918, xxi, 59; 1918, xxii, 157; and 1919, xxiv, 295.

Mall, F. P. Amer. Jour. Anat., 1902-03, ii, 315.

Mallory, F. B. Jour. Exper. Med., 1900, v, 1.

Masing, E., und Morawitz, P. Deutsch. Arch. f. klin. Med., 1909-10, xcviii, 301.

Masing, E. Arch. f. exper. Path. u. Pharm., 1911, lxvi, 71.

Maximow, A. Arch. f. mikr. Anat., 1905, lxvii, 680. Arch. f. mikr. Anat., 1908-09, lxxiii, 444.

Meves, F. Arch. f. mikr. Anat., 1910-11, lxxvi, 683.

Meyer, E., and Butterfield, E. E. Arch. Int. Med., 1914, xiv, 94.

Meyer, E., and Heineke, A. Deutsch. Arch. f. klin. Med., 1906-07, lxxxviii, 435.

Meyer, E., and Rieder, H. Atlas der klin. Mikroskopie des Blutes, 2 Aufl., Leipzig, 1907, F. C. W. Vogel, p. 44.

Miller, J. L. Jour. A. M. A., 1917, lxix, 765.

Miller, S. R. Bull. Johns Hopkins Hosp., 1914, xxv, 317.

Miller, J. A., and Reed, M. A. Arch. Int. Med., 1912, ix, 609.

Milroy, T. H., and Malcolm, J. Jour. Physiol., 1899-1900, xxv, 105.

Minot, C. S. In Manual of human embryology (Keibel and Mall), 1912, ii, 533; also 505.

Minot, G. R., and Lee, R. I. Boston Med. and Surg. Jour., 1917, clxxvii, 761. Arch. Int. Med., 1916, xviii, 474.

Mollier, S. Arch. f. mikr. Anat., 1910-11, lxxvi, 608.

Morawitz, P. Ergebn. d. inn. Med. u. Kinderh., 1913, xi, 277. Arch. f. exper. Path. u. Pharm., 1908-09, lx, 298. Blut und Blutkrankheiten. In Handb. d. inn. Med. (Mohr & Staehelin), Berlin, 1912, iv, 92-346.

Morawitz, P., und Itami, S. Deutsch. Arch. f. klin. Med., 1910, c. 191.

Morris, D. H. Jour. Exper. Med., 1914, xx, 379.

Morris, R. S. Arch. Int. Med., 1915, xv, 514. The blood. In Clin. laboratory methods, N. Y., 1913, 226.

Morris, R. S., and Boggs, T. R. Arch. Int. Med., 1911, viii, 806.

Morris, R. S., and Thayer, W. S. Arch. Int. Med., 1911, viii, 581.

Muir, R. Jour. Path. and Bacteriol., 1901, vii, 161.

Müller, F. In Handb. d. Biochem. (Oppenheimer), Jena, 1909, i, 662; and 1913, Erganzungsbd., 113.

Muller, H. F. Deutsch. Arch. f. klin. Med., 1891, xlviii, 47.

Murphy, J. B,. and Ellis, A. W. M. Jour. Exper. Med., 1914, xx, 397.

Murphy, J. B., and Sturm, E. Jour. Exper. Med., 1919, xxix, i, 25, 31, 35.

Myers, V. C., and Fine, M. S. Chemical composition of the blood in health and disease. Post-Graduate, N. Y., 1915, xxx, 39.

Naegeli, O. Blutkrankheiten und Blutdiagnostik, Veit & Co., Leipzig, 1912, 2nd Edition.

Nakahara, W. Jour. Exper. Med., 1919, xxix, 17 and 83.

Nasmith, G. G., and Graham, D. A. L. Jour. Physiol., 1906-07, xxxv, 32.

Nasmith, G. G., and Harrison, F. C. Jour. Exper. Med., 1910, xii, 282.

Neumann, E. Centralb. f. d. med. Wissensch., 1868, 689.

Opie, E. L. Amer. Jour. Med. Sc., 1904, cxxvii, 217, 477, 988. Jour. Exper. Med., 1905, vii, 316; 1906, viii, 410; and 1907, ix, 391, and 414.

Ottenberg, R., and Rosenthal, N. Jour. A. M. A., 1917, lxix, 999.

Ottolenghi, D. Atti della Royal. Accad. delle Sci. di Torino, 1901, xxxvi, 611; and Arch. ital. d. biol., 1902, xxxvii, 73.

Palmer, W. W. Jour. Biol. Chem., 1918, xxxiii, 119.

Paltauf, R., Freund, E., and Sternberg, C. Die Pathologie des Blutes. Handb. d. allg. Pathol. (Krehl & Marchand), Leipzig, 1912, ii, 1, 1-217.

Pappenheim, A. Grundriss der hämatologischen Diagnostik u. praktischen Blutuntersuchung. Leipzig, 1911, W. Klinckhardt. Atlas der menschlichen Blutzellen, Jena, 1905-12, G. Fischer. Clinical examination of the blood and its technic. New York, 1912, W. Wood & Company. Allgemeine Einleitung. Die Blutveränderunger im allgemeinen, ihr Wesen, Zustandekommen, symptomatologischer Wert u. diagnostische Bedeutung. In Spez. Path. u. Therap. inn. Krankh. (Kraus u. Brugsch), Berlin u. Wien, 1915, viii, 1-55. Die Zellen der leukämischen Myelose (Leukämie-Zellen). Tafeln zum Studium der normalen und pathologischen menschlichen Blutzellen. Text u. Atlas, Jena, 1914, G. Fischer. Technik der klin. Blutuntersuchung. Für Studierende und Aerzte. Berlin, 1911, J. Springer. Die kardinalen Blutsymptome. Folia Hæmatol., Berlin, 1914, xviii, 227-239. Vergleichende Untersuchungen über die elementare Zusammensetzung des rothen Knochenmarkes einiger Säugethiere. Virchow's Archiv., Berlin. 1899. clvii, 19-77.

Parmentier, E. Maladies du sang. Paris, J. B. Baillière et fils. [Nouv. Traité de Méd. de Thérap., xxvi.]

Pearce, R. M., and Austin, J. H. Jour. Exper. Med., 1912, xvi, 780.

Pearce, R. M., and Austin. J. H., and Eisenbrey, A. B. Jour. Exper. Med. 1912, xvi, 375.

Pearce, R. M., Krumbhaar, E. B., and Frazier, C. H. The spleen and anemia, 1918.

Photakis, B. Archiv. f. path. Anat. (Virchow), Berlin, 1915, ccxix, 41.

Pohl, J. Arch. f. exper. Path. u. Pharmakol., 1888-89, xxv, 31.

Renaut, J. Arch. d'Anat. micr., 1906-07, ix, 495.

Rieder, H. Beiträge zur Kenntniss der Leucocytose und verwandter zustände der Blutes, Leipzig, 1892, 189.

Rindfleisch, G. E. Arch. f. mikr. Anat., 1879, xvii, 1 and 21.

Ritz, H. Folia Hæmat., 1909, viii, 186.

Robertson, O. H. Jour. Exper. Med., 1917, xxvi, 221.

Robertson, O. H., and Bock, A. V. Jour. Exper. Med., 1919, xxix, 139 and 155.

Roger, H., and Josue, O. Presse méd., 1897, v, 113.

Roth, O. Ztschr. f. klin. Med., 1912, lxxvi, 23.

Rous, F. P. Jour. Exper. Med., 1908, x, 238, and 329.

Rous, P., and Robertson, O. H. Jour. Exper. Med., 1917, xxv, 651, 665.

Rowley, M. W. Jour. Exper. Med., 1908, x, 78.

Ruh, H. O. Metaplastic bone and marrow formation in vessel walls. Cleveland Med. Jour., 1913, xii, 723.

Sahli, H. Untersuchung des Blutes. In Lehr. d. klin. Untersuchungsmethoden, 5 Aufl., Leipzig u. Wien, 1909, 825-981.

Sailer, J., and Taylor, A. E. Internat. Med. Mag., 1897, vi, 404.

Schauman, O., und Rosenquist, E. Ztschr. f. klin. Med., 1898, xxxv, 126 and 315.

Schiff, E. Ztschr. f. Heilk., 1890, xi, 17.

Schleip, K. Hematological atlas, with a description of the technic of blood examination. English adaptation of text of F. E. Sondern. 1908, Rebman Co., New York.

Schneider, E. C., and Havens, L. C. Amer. Jour. Physiol., 1915, xxxvi, 239; and 1914-15, xxxvi, 380.

Schneider, J. P. Arch. Int. Med., 1916, xvii, 32.

Schmidt, P. München. med. Wchnschr., 1903, l, 549-553.

Schridde, H. Centralb. f. allg. Path. u. path. Anat., 1908, xix, 865. Anat. Anz., 1912, xlii, 514.

Schridde, H., und Naegeli, O. Die hæmatologische Technik. Jena, 1911, G. Fischer.

Schulz, G. Deutsch. Arch. f. klin. Med., 1893, li, 234.

Schumm, O. Beitr. z. chem. Phys. u. Path., 1904, iv, 442. Deutsch. med. Wchnschr., 1905, xxxi, 1831.

Sellards, A. W., and Baetjer, W. A. Bull. Johns Hopkins Hosp., 1918, xxix, 135.

Sellards, A. W., and Minot, G. R. Jour. Med. Research, 1916, xxix, 469; and 1917, xxxii, 161.

Selling, L. Beitr. z. path. Anat. u. z. allg. Path., 1911, li, 576. Bull. Johns Hopkins Hosp., 1910, xxi, 33. Johns Hopkins Hosp. Reports., Monographs, 1913, No. 2.

Sherrington, C. S. Proc. Royal Soc., London, 1894, lv, 161.

Shipley, P. G. Folia Hæmat., 1915, xx, 59.

Silverman, J. G. Univ. of Pennsylvania Med. Bull., 1904-05, xvii, 22.

Silvestri, T. Milza e Eritropoiesi. Patologica, 1913, v. 145.

Starling, E. H., Barcroft, J., and Hardy, W. B. Rep. Brit. Ass. Adv. Sc., 1913, London, 1914, 260.

Stengel, A. Diseases of the blood. Progres. Med., Phila. & N. Y., 1914, ii, 301.

Sternberg, C. Ergebn. d. allg. Path. u. path. Anat., Wiesbaden, 1905, ix, 2 Abt., 360-517.

Stewart, G. N. Jour. Physiol., 1899, xxiv, 514.

Stockard, C. R. Amer. Jour. Anat., 1915, xviii, 227 and 286.

Stone, W. J., and Schottstaedt, R. Arch. Int. Med., 1912, x, 8.

Taylor, H. D. Jour. Exper. Med., 1919, xxix, 41.

Taylor, H. D., Witherbee, W. D., and Murphy, J. B. Jour. Exper. Med., 1919, xxix, 53.

Thayer, W. S. Arch. Int. Med., 1911, vii, 223.

Thomas, M. W., Taylor, H. D., and Witherbee, W. D. Jour. Exper. Med., 1919, xxix, 75.

Thomsen, O. Hospitalstidende, 1919, lxii, 161.

Tower, R. W., and Herm, C. F. Proc. Soc. Exper. Biol. and Med., 1916-17, xiv, 51.

Türk, W. Vorlesungen über klin. Hämatologie. 1. Teil. Wien, 1904. W. Braunmüller, ii. Teil, 1912.

Van Der Stricht, O. Arch. de biol., 1892, xii, 199, and 251; and 1891, xi, 19.

Van Kostanecki, K. Anat. Heft., 1891, i, 303.

Van Nuys, F. Boston Med. and Surg. Jour., 1907, clvi, 390.

Van Slyke, D. D. Jour. Biol. Chem., 1918, xxxiii, 127.

Viault. Compt. rend. Acad. d. Sc. 1890, cxi, 917; and 1892, xciv, 1562. Compt. rend. Soc. de Biol., 1892, ix, Ser. iv, 569.

Von Noorden, C. Charité Ann., 1891, xvi, 224.

Wack, P. Deutsch. Arch. f. klin. Med., 1914, cxv, 596.

Walz, K. Centralb. f. Pathol., 1901, xii, 966.

Ward, G. R. Bedside hæmatology. Philadelphia and London, 1914, W. B. Sounders Co.

Warburg, O. Zeits. f. physiol. Chem. (Hoppe-Seyler's), 1910, lxvi, 305; and 1912, lxxvi, 331.

Warfield, L. M. Jour. A. M. A., 1915, lxiv, 1296.

Webster, R. W. The blood. Diagnostic methods. 3rd ed., Philadelphia, 1913, 376.

Weidenreich, F. Anat. Anz., 1908, xxxii, 81. Arch. f. mikr. Anat., 1908, lxxii, 209. Ergebn. d. Anat. u. Entwickelungsgeschichte, 1909, xix, 527.

Wells, C. W. Jour. Inf. Diseases, 1917, xx, 219.

Werigo. Ann. de l'Inst. Pasteur, 1892, vi, 478.

Whipple, G. H., and Hooper, C. W. Jour. Exp. Med., 1913, xvii, 612.

Wickline, W. A. Military Surgeon, 1908, xxiii, 282.

Williamson, C. S. Arch. Int. Med., 1916, xviii, 505.

Winternitz, P. Arch. f. exper. Path. u. Pharm., 1895, xxxv, 77.

Wolff, A. Berl. klin. Wchnschr, 1901, xxxviii, 1290.

Wright, J. H. Virchow's Arch. f. path. Anat., 1906, clxxxvi, 55. Journal of Morphology, 1910, xxi, 263. *In* Manual of human embryology (Keibel and Mall), 1912, Vol. II, 523.

Wright, J. H., and Kinnicutt, R. Jour. A. M. A., 1911, lvi, 1457.

Wright, J. H., and Minot, G. R. Jour. Exper. Med., 1917, xxvi, 395.

Ziegler, K. Diagnostik der Krankheiten des Blutes. *In* Lehrb. d. klin. Diagnostik (P. Krause), 2 Aufl., Jena, 1913, G. Fischer, 404.

Zinsser, H., and Tsen, E. Jour. Immunol., 1916-17, ii, 247.

Zuntz, N., und Schumburg, W. E. F. Studien zu einer Physiologie des Marsches, Berlin, 1901.

Blood Examination

Aebly, J. Cor.-Bl. f. schweiz. Aerzte, Sept. 11, 1919, xlix, 1393.

Alder, A. Cor.-Bl. f. schweiz. Aerzte, June 21, 1919, xlix, 925; abstr. Jour. A. M. A., August 23, 1919, lxxiii, 649.

Arneth, J. Deutsche med. Wchnschr., Jan. 29, 1920, xlvi, 119.

Aschoff, L., and Kiyono. Folia Hæmatolog., Leipzig, 1913, xv, 1. Theil, 383.

Audain, G. Presse méd., April 24, 1919, xxvii, 216; abstr. Jour. A. M. A., June 7, 1919, lxxii, 1707.

Barker, L. F. Monographic Medicine, Vol. III, p. 35, D. Appleton & Co., New York. Johns Hopkins Hosp. Bull., 1894, v, 93.

Bauer, J., und Aschner, B. Deutsch. Arch. f. klin. Med., Sept., 1919, cxxx, 172; abstr. Jour. A. M. A., May 22, 1920, lxxiv, 1491.

Bètances, L. M. Arch. d. mal. du. Coeur, Feb., 1920, xiii, 66.

Bierring, K. Ugesk. f. Læger, November 18, 1920, lxxxii, 1445.

Bilis, A. S., Shishov, B. A., and Silberstein, E. Amer. Jour. Surg., Jan., 1919, xxxiii, 9.

Bing, H. I. Ugesk. f. Læger, Sept. 18, 1919, lxxxi, 1483.

Bockhorn, M. Ztschr. f. klin. Med., lxxxix, 304, 1920; abstr. Jour. A. M. A., Oct. 23, 1920, lxxv, 1169.

Bunting, C. H. Amer. Jour. Med. Sci., 1911, cxlii, 698.

Bürker, K. Arch. f. d. ges. Physiol., Bonn, 1913, cliii, 128.

Cabot, R. C. Amer. Jour. Med. Sci., 1913, cxlv, 335. Boston Med. and Surg. Jour., 1894, cxxx, 277. Jour. Med. Research, Boston, 1903, ix, 15.

Cooke, W. E. Jour. Path. and Bacter., Cambridge, 1914-15, xix, 494.

Cook, J. E., and Meyer, J. Arch. Int. Med., 1915, xvi, 644.

Deetjen, H. Handb. d. biochem. Arbeitsm., 1912, vi, 383.

Downey, H. Folia Hæmatol., Leipzig, Arch., 1913, xv, 1. Theil, 25; and 1915, xix, 148.

Dreyer, G., Bazett, H. C., and Pierce, H. F. Lancet, Sept. 18, 1920, ii, 588.

Dreyer, G., and Gardner, A. D. Lancet, Oct. 18, 1919, ii, 687.

Duke, W. W. Johns Hopkins Hosp. Bull., 1912, xxiii 144. Arch. Int. Med., 1913, xi, 100. Jour. A. M. A., 1915, lxv, 1600.

Dunger, R. München. med. Wchnschr., 1910, lvii, 1942.

Ehrlich, P. Farbenanalytische Untersuchungen z. Hist. u. Klink des. Blutes, 1. Theil, Berlin, 1891.

Emerson, C. P. The blood. *In* Clinical Diagnosis, Philadelphia, 1906, 392.

Eustis, A. Jour. A. M. A., 1913, lxi, 1984.

Feigl, J. Zentralbl. f. inn. Med., Jan. 10, 1920, xli, 17; abstr. Jour. A. M. A., March 27, 1920, lxxiv, 926.

Friedman, G. A. Amer. Jour. Med. Sci., Oct., 1919, clviii, 545.

Galt, H. M. Brit. Med. Jour., London, 1913, ii, 1367.

Gay, L. N. Arch. Int. Med., May, 1919, xxiii, 603.

Gehrig, R. P. Ztschr. f. exper. Path. u. Therap., Berlin, 1915, xvii, 161.

Geyser, A. C. N. Y. Med. Jour., June, 1919, cix, 978.

Giffin, H. Z., and Sanford, A. H. Jour. Lab. and Clin. Med., May, 1919, iv, 465.

Giffin, H. Z. Amer. Jour. Med. Sci., Nov., 1919, clviii, 618.

Gironi, U. Mitt. a. d. Grenzgeb. d. Med. u. Chir., Jena, 1913, xxv, 229.

Goldscheider, A., and Jacob, P. Ztschr. f. klin. Med., Berlin, 1894, xxv, 373.

Gowers, W. R. Trans. Clin. Soc., London, 1879, xii, 64.

Grawitz, E., and Gruneberg. Die Zellen des menschlichen Blutes im ultravioletten Lichte. Leipzig, 1906, G. Thieme.

Greene, C. L. Medical diagnosis, 4th Ed., P. Blakiston's Sons & Co., Phila., Pa., pp. 110-143.

Gruner, O. C. Practitioner, London, Nov., 1919, ciii, 381.

Gulland, and Goodall. The blood; a guide to its examination and to the diagnosis and treatment of its diseases, Edinburgh and London, 1912, Green & Sons.

Harms, F. H. Penna. Med. Jour., Athens, Pa., 1915, xix.

Harrop, A., Jr. Arch. Int. Med., June, 1919, xxiii, 745.

Harvey, W. F. Indian Jour. Med. Research, Jan., 1920, vii, 479.

Hastings, T. W. Jour. A. M. A., 1907, xlviii, 1749.

Helly, K. Ergebn. d. allg. Path., Wiesbaden, 1914, xvii, Abt. 1, 1-137.

Hill, L. W. Boston Med. and Surg. Jour., 1914, clxx, 792.

Howell, W. H. Jour. Morphol., Boston, 1890, iv, 57.

Hoxie, G. H. Interstate Med. Jour., St. Louis, 1913, xx, 1049.

Jantke, E. Vergleichende Untersuchungen ueber den Wert einiger Methoden der klin. Hämoglobinbestimmung. Bonn, 1913, E. Eisele.

Jordan, H. E. Proc. Soc. Exper. Biol. and Med., N. Y., 1914-15, xii, 167.

Jorgensen, G. Hospitalstid., April 2, 1919, lxii, 432; abst. J. A. M. A., June 7, 1919, lxxii, 1712.

Juspa, V. Folia Hæmatol., Leipzig, 1914, xvii, 429.

Kambe, H., and Komiya, E. Amer. Jour. Physiol., August, 1920, liii, 1.

Katzenstein, M. B. Jour. A. M. A., 1911, lvii, 22.

Kiyono, K., and Nakanoin, T. Acta scholæ med. univ. imp., Kioto, Jan., 1919, iii, 55; abstr. Jour. A. M. A., July 26, 1919, lxxiii, 305.

Lamson, P. D. Jour. Pharm. and Exper. Therap., Sept., 1920, xvi, 125.

Langer, H. Deutsch. med. Wchnschr., Jan. 8, 1920, xlvi, 47.

Leonard, G. F. Jour. Med. Soc. New Jersey, Oct., 1919, xvi, 354.

Lilliendahl-Peterson, N. Berl. klin. Wchnschr., 1914, li, 551.

Loeper, M. Progrès méd., Jan. 25, 1920, xxxv; abstr. Jour. A. M. A., April 3, 1920, lxxiv, 986.

McJunkin, F. A., and Charlton, A. G. Arch. Int. Med., Sept., 1919, xxiv, 295.

Meyer, E., and Butterfield, E. E. Arch. Int. Med., 1914, xiv, 94.

Michaelis, L., and Wolff, A. Deutsch, med. Wchnschr., Leipzig u. Berlin, 1901, xxvii, 651.

Morris, R. S. Johns Hopkins Hosp. Bull., 1907, xviii, 198. Arch. Int. Med., 1909, iii, 93.

Morris, R. S., and Thayer, W. A. Arch. Int. Med., 1911, viii, 581.

Murphy, I. J. Journal-Lancet, Feb. 15, 1920, xl, 106.

Naegeli, O. *In* Spez. Pathol. u. Therap. inn. Krankh. Kraus u. Brugsch, Berlin u. Wien, 1915, Vol. VIII, 57.

Osler, Sir W. The third corpuscle of the blood. Philadelphia, 1883; repr. from Med. News, Philadelphia, 1883, xliii, 701. Cartwright Lectures, Philadelphia, 1886; repr. from Med. News, Philadelphia, 1886, xlviii, 365, 393 and 421.

Palmer, W. W. Jour. Biol. Chem., 1918, xxxiii, 119.

Petzetakis, M. Lyon chir., May-June, 1919, xvi, 255.

Plaut, F. München. med. Wchnschr., March 5, 1920, lxvii, 279; abstr. J. A. M. A., Sept. 11, 1920, lxxv, 776.

Plesch, J. Ztschr. f. exper. Path. u. Therap., Berlin, 1907, iv, 867.

Pratt, J. H. Jour. A. M. A., 1905, xlv, 1999.

Price-Jones, C. Jour. Path. and Bacter., Dec., 1920, xxiii, 371.

Reichart, A. Wien. klin. Wchnschr., Jan. 8, 1920, xxxiii, 45.

Rieder, H. Beiträge zur Kenntniss der Leukocytose u. verwandter Zustände des Blutes, Leipzig, 1892, F. C. W. Vogel.

Roemmele, A., and Sweet, R. Lancet, London, 1913, ii, 384.

Rogers, J. B. Bull. Iowa Inst., Des Moines, 1915, xvi, 132.

Rohrer, F. Cor.-Bl. f. schweiz. Aerzte, June 28, 1919, xlix, 971.

Runge, W. München. med. Wchnschr., Aug. 13, 1920, lxvii, 953; abstr. Jour. A. M. A., Dec. 11, 1920, lxxv, 1685.

Schilling, V. Ztschr. f. klin. Med., 1920, lxxxix, 1; abstr. Jour. A. M. A., Oct. 16, 1920, lxxv, 1102.

Schneider, E. C., and Havens, L. C. Amer. Jour. Physiol., 1914-15, xxxvi, 380.

Schwarz, E. Ergebn. d. allgem. Path., Wiesbaden, 1914, xvii, Abth. i, 138.

Stäubli, C. Ergebn. d. inn. Med. u. Kinderh., Berlin, 1910, vi, 192. Arch. f. exper. Path. u. Pharmacol., Leipzig, 1897, xxxix, 385.

Thayer, W. S. Johns Hopkins Hosp. Bull., 1893, iv, 37. Arch. Int. Med., 1911, vii, 223.

Thoma, R. Arch. f. path. Anat., Berlin, 1882, lxxxvii, 201.

Toison, J. J. d. Sc. Med. de Lille, 1885, vii, 97.

Turk, W. Wien klin. Wchnschr., 1902, xv, 715, 749.

Veillon, E. Arch. f. exper. Path. u. Pharmakol., Leipzig, 1897, xxxix, 385.

White, H. L., and Watson, T. Jour. Lab. and Clin. Med., Oct., 1920, vi, 45.

Wood, F. C., and others. Symposium on clinical significance of blood examination. International Clinics, 1919, iii, 120.

Wright, J. H., and Kinnicutt, R. Jour. A. M. A., 1911, lvi, 1457.

Wyss, O. Schweiz. med. Wchnschr., March 18, 1920, l, 226; abstr. Jour. A. M. A., June 12, 1920, lxxiv, 1680.

CHAPTER II

THE ANEMIAS

BY CHARLES LYMAN GREENE, M.D.

Notes on the anemias, p. 780:—Variations in blood-pictures, p. 780; Chief types of anemia, p. 780; Certain etiologic factors in anemia, p. 781; General symptomatology of the anemias, p. 782—Preliminary discussion, p. 782; Outward symptoms, p. 782; Bright's disease, p. 782; Syphilis, p. 783; Malignant disease, p. 783; Effect of certain heart lesions, p. 783; Dyspnea, p. 783; Circulatory system, p. 783; Anemic murmurs, p. 783; Therapeutic suggestions, p. 784; Chronic congenital asthenia, p. 784; Nervous system, p. 785; Cause of divorce, p. 785; Gastro-intestinal tract, p. 785; General nutrition, p. 785; Eye, p. 785.

The anemias, p. 786—Hemolysis and regeneration, p. 786:—Pathologic hemolysis, p. 787; Blood-picture in hemolysis, p. 787; Blood regeneration in hemolytic anemias, p. 787; Blood-picture in severe hemolytic anemias, p. 788; Origin and destruction of the leukocytes, p. 788; Destruction of the granular leukocytes, p. 788.

Chlorosis, p. 789:—Definition, p. 789; Etiology, p. 789:—Age and sex, p. 789; Congenital asthenic, p. 789; Older theories of causation, p. 790; Unfavorable environment, p. 791—Symptomatology, p. 791:—Clinical history, p. 791; Subjective symptoms, p. 791:—Gastro-intestinal tract, p. 792; Constipation, p. 792; Disturbances of menstruation, p. 792; Cardiovascular system, p. 792—Physical findings, p. 793:—Outward signs, p. 793; Superficial fat, p. 793; Dyspnea on exertion, p. 793; Warning, p. 794—Laboratory findings and special examination, p. 794:—Blood, p. 794—Diagnosis, p. 794:—Anemia from malignant disease, p. 795; Anemias of tuberculosis, p. 796; Posthemorrhagic anemias, p. 796; Anemia of renal disease, p. 796; Anemias due to infections, p. 796—Complications and sequelae, p. 797:—Gastric ulcer, p. 797; Sinus and venous thrombosis, p. 797; Myocardial insufficiency, p. 797—Treatment, p. 797:—General factors in therapy of chlorosis, p. 798:—Subordinate and contributory factors in treatment, p. 798; Flatulence in anemias, p. 799; Constipation, p. 799; Fresh air, sunshine and regulated exercise, p. 800; Oral administration of iron, p. 800; Hypodermic use of iron, p. 802; Arsenic, p. 802; Manganese, p. 802; Hydrotherapy, p. 803; Exercise in chlorosis, p. 803; Treatment of nervous symptoms of chlorosis, p. 803—Prognosis, p. 804; Pathology, p. 804.

Idiopathic aplastic pernicious anemia, p. 804:—Definition, p. 804; Etiology, p. 804; Symptomatology, p. 805; Differential diagnosis, p. 805; Treatment, p. 806; Pathology, p. 807.

Myelophthisic anemia, p. 807:—Definition, p. 807.

Simple chronic anemia (associated with defective hematopoiesis), p. 807:—Definition, p. 807; Etiology, p. 807; Treatment, p. 807.

Acute posthemorrhagic anemia, p. 808:—Definition, p. 808; Symptomatology, p. 808.

Chronic posthemorrhagic anemia, p. 809:—Definition, p. 809; Etiology, p. 809; Symptomatology, p. 809; Diagnosis, p. 809; Treatment and prognosis, p. 809.

Addisonian pernicious anemia, p. 810:—Definition, p. 810; Etiology, p. 810; Symptomatology, p. 811:—Clinical history, p. 811—Diagnosis, p. 815; Complications, p. 815; Association with other diseases, p. 816; Clinical varieties and types, p. 816; Treatment, p. 816; Prognosis, p. 822; Pathology, p. 823.

Hemolytic anemia (other than Addisonian pernicious anemia), p. 823:—Dibothriocephalus anemia, p. 824; Hemolytic anemia of pregnancy, p. 825; Acute hemolytic anemia, p. 825.

NOTES ON THE ANEMIAS

In connection with the anemias, as in the case of certain other disease groups, there has been in the past an unfortunate tendency to dignify any minor variations of the clinical type by describing it as a syndrome or even as a distinct disease, usually with the name of some clinician affixed.

This deplorable custom should be done away with so far as possible in the future inasmuch as it tends to force out of their proper clinical relationship minor variants of clinical types. Indeed the custom serves for the most part to lend to the observer at fault a kudos usually wholly undeserved. Furthermore, it burdens and confuses the minds of students and physicians alike.

Objection may be raised properly also to the tendency to formulate classifications based upon the preference or the peculiar theories of individuals, for these also serve in great measure to confuse the mind by their multiplicity and our knowledge of the pathogenesis of the anemias, and indeed of the fundamental factors in the genesis of the blood constituents, is too far from being accurate and proven to justify anything approaching dogmatic statement.

Hematology has become of great importance in medicine. Nevertheless, as regards the acquisition of fundamental knowledge concerning the actual cause of anemias, the advance of late years has been disappointing. At the present time there exists a wide diversity of views and far too many of the statements in print represent merely individual opinion often largely or wholly theoretic.

Variations in Blood-pictures.—One must remember that the element of transition plays undoubtedly a large part in the clinical picture attending the development and course of the anemias, and that upon this action depends in a considerable measure the wide variations therein observed. In the past unquestionably there has been too great a tendency to classify such transition pictures, or slight variations from the classical types, as individual ailments.

Another objectionable feature of our attitude in the past with respect to the studies of the blood diseases has been a tendency to over-emphasize the diagnostic significance and importance of certain individual morphologic departures from the normal in the cellular elements of the blood. The presence of basophils, certain degrees of anisocytosis, polychromasia and the like are of great value to the observer in many instances and may form an important part of a clinical picture, but existing alone in cases lacking the more important or cardinal symptoms of this or that type of anemia, their importance is trivial. Such conditions, if present, should be recorded and reported but that is all. Specific significance and pathognomonic meaning must not be attributed to them.

Chief Types of Anemia.—The three chief types of anemia proper are those dependent upon (*a*) defective blood formation, (*b*) excessive blood destruction, and (*c*) association with acute, chronic, or chronically intermittent blood loss.

In chlorosis, or in the so-called simple chronic anemias, the usually dominant blood defect is a deficiency of hemoglobin in the erythrocyte and a consequent loss of the ability of the blood to make its proper combinations with oxygen. In such cases the hemoglobin content of the individual cell may be reduced to a figure so low as to make especially accurate determinations necessary, whereas the number of erythrocytes per cubic millimeter may be normal or relatively little reduced.

In the ordinary forms of secondary anemia, there is more likely to be a rough equality maintained between the hemoglobin deficit and the erythrocyte deficiency.

In true Addisonian pernicious anemia, on the other hand, the reduction in the number of red cells per cubic millimeter is greater proportionately than the loss of hemoglobin. Indeed the individual red cell appears to contain a relative excess of this substance in direct contrast to the appearance of the erythrocyte in chlorosis.

Certain Etiologic Factors in Anemia.—Our knowledge of the etiology of the anemias seems still to be unsatisfactory and but crudely and imperfectly worked out. In the case of the commonest form, namely, chlorosis, known since the days of Hippocrates and in times before him, we have yet to learn the true basic etiologic factors.

At most we can assemble only a group of contributive or predisposing etiologic conditions and affirm with some positiveness the connection of this peculiar ailment with the period of sexual development in the female.

In the case of the secondary anemias a specific etiologic factor oftentimes can be determined, inasmuch as in large measure these are induced by the activity of the toxins of specific bacteria or demonstrable primary pathologic processes of nonbacterial origin and yield with the cessation of infection under proper treatment.

At the present time a very large group of secondary anemias must be regarded as the result of concealed septic foci, but so far as one can determine these more important etiologic factors are not proven to be operative in Addisonian pernicious anemia or even in the aplastic form of chronic progressive fatal anemia, nor can they be held to operate primarily in the case of chlorosis.

In Addisonian pernicious anemia, to which, by the way, the term "Biermer's anemia" [*] is absolutely inapplicable, the outstanding clinical feature lies in the continued or recurring hemolytic process resulting in actual blood destruction which is attended by attempts on the part of the blood-forming tissues to overcome the handicap to the organism through intensive efforts at regeneration. These result in the appearance in the blood of extraordinary and bizarre forms of cells, for the most part of the immature type.

In certain instances the anemia of nitrobenzol poisoning or that of bothriocephalus invasion, the picture may be almost identical with that of true Addisonian anemia but its cause is discoverable and removable and the cure obtainable.

---

[*] It is to be hoped that in the future more care will be taken with respect to the maintenance of the rights of the dead in the proper crediting of medical discoveries made and announced to the profession. In the past physicians of all countries have been too ready to accept the substitution of the names of certain great observers who may merely have elaborated the fundamental work of other men and thereby permit the greatest injustice to be done to the original discoverer. The application of Biermer's name to Addisonian anemia and the failure to credit Francis H. Welch with the discovery and adequate description of syphilitic aortitis constitute two of the most outstanding examples of such injustice. Biermer's article was written in 1868, nearly 20 years after Addison, in 1849, had described progressive pernicious anemia of the plastic type. Francis H. Welch, sometime Professor of Pathology at Neteley, reported on and described syphilitic mesaortitis, in 1875. Döhle wrote in 1895, and Heller in 1899; yet we find this disease referred to constantly as the "Döhle-Heller" aortitis.

General Symptomatology of the Anemias.—PRELIMINARY DISCUSSION.—For the greater part the production of symptoms in all cases of anemia is dependent fundamentally and chiefly upon the loss of the oxygen-carrying and combining power of the blood and the consequent interference with cell nutrition and function. The degree of impairment of function varies widely in the different forms of anemia, being so slight as to be negligible in the milder varieties and of a most serious nature in the pernicious anemias and leukemia. Furthermore, in certain of the fatal progressive forms toxins are developed which in themselves tend to produce symptoms of the greatest gravity.

OUTWARD SYMPTOMS.—In general the most striking outward symptom of anemia is pallor, and in the case of profound acute blood loss this is seen as a waxy dead whiteness of the skin and pale mucous membranes. In Addisonian pernicious anemia the high grade of hemolysis present is responsible no doubt for the peculiar lemon-yellow pallidity so commonly observed in the more advanced or well-established cases of this disease, a color so striking as almost to be pathognomonic when present in its typical form.

This striking outward symptom may be wholly lacking, however, in the progressive pernicious anemia of the aplastic, nonhemolytic, nonregenerative type, in which there may be a simple blanching of the skin and mucous membranes or a slight sallowness such as is likely to be observed in chronic or intermittent blood loss and resulting secondary anemias.

In chlorosis the typical color, from which the disease derives its name, is a peculiar greenish sallowness, but it should be stated that this typical color is often lacking in this disease and furthermore that a not inconsiderable number of cases of chlorosis show red cheeks (chlorosis rubra).

The same statement may be made with regard to leukemia, in which pallor is usually marked, associated with a grayish tint of the skin. The writer has seen repeatedly cases of advanced leukemia in persons with a delicate skin in whom there was the superficial appearance of full-bloodedness and high color.

These statements being accepted, it is true nevertheless that in no case of severe anemia do we lack outward proof of the presence of that condition inasmuch as whatever the color of the skin itself, the mucous membranes will show pallor if the anemia be marked. In other words persons may be pale, yet not anemic; ruddy, yet profoundly anemic; but never anemic, with *normal* color in the visible mucous membranes. It must be borne in mind always that mere pallor is extremely common in indoor workers and in delicate persons even though the blood may be nearly or quite normal. The conjunctivæ, the lips, the buccal and pharyngeal mucous membranes best show the relative pallor indicative of actual anemia. The bed of the finger nail and the lobe of the ears are also points at which pallor is marked in such cases.

BRIGHT'S DISEASE.—In Bright's disease with anemia the color variations associated with the different types and stages of the ailment are marked. In acute Bright's disease with general edema one meets with the curious pasty white skin. In these cases the peculiar dead white skin of the legs may be traversed and overlaid by venules in such a manner as to justify the old-fashioned term "marble-like" as applied to the underlying edema present. Certain forms of Bright's disease of the chronic type result in a peculiar fawn-colored skin which is quite characteristic.

The ordinary form of chronic interstitial nephritis, even though it be associated with a considerable degree of anemia, may give little evidence of it outwardly, the appearance of the patient being oftentimes that of robust and even florid health. It may be added that the degree of anemia present in the different forms of Bright's disease, or in any one form, varies very greatly, being ordinarily moderate and of the secondary type, but in rare instances reaching the grade of the pernicious form.

SYPHILIS.—In general the anemia of syphilis is of the secondary type and presents no striking characteristics, but in certain congenital and tertiary cases the anemia may be marked and carried over long periods of time with the result that there is produced in the skin, of the face especially, a peculiar sallow pallor difficult to describe yet quite characteristic and when once seen not likely to be forgotten.

MALIGNANT DISEASE.—In malignant disease the degree of anemia varies widely, but in some instances reaches a high grade and, especially in certain cases of carcinoma of the stomach with metastases in the liver, may be so extreme as to simulate closely Addisonian pernicious anemia. In such cases, however, the outward appearance is usually that produced by the secondary anemia of malignancy, a peculiar earthy muddy pallor rather than the clear lemon-yellow tint of plastic progressive pernicious anemia.

EFFECT OF CERTAIN HEART LESIONS.—In mitral regurgitation and especially in mitral stenosis, or in a combination of these lesions, an existing anemia may be masked by the misleading redness of the patient's cheeks and lips. This redness is not likely to deceive the experienced eye, however, inasmuch as it is darker than the flush of health and, in the lips, more intense. Frank advanced cases of aortic regurgitation may, by the curious pallor which most of them carry, bring about an erroneous assumption of existing anemia where none is present.

DYSPNEA.—Only in the higher grades of anemia are we likely to find decided dyspnea which is attributable fairly to the condition of the blood itself and indeed in many instances it is difficult to determine to what extent an existing exertion dyspnea is to be credited to the accompanying myocardial weakness so often present in severe chlorosis and in the pernicious and severe secondary anemias. The symptom is peculiarly marked in chlorosis and in the plastic and aplastic pernicious anemias.

CIRCULATORY SYSTEM.—In all severe types of anemia of long duration the myocardium must suffer to a greater or less degree, and one finds accordingly symptoms attributable to heart muscle insufficiency of varying degree in a large number of cases. Palpitation, syncopal attacks and precordial oppression are often present and constitute sometimes most troublesome complications.

The heart itself is often dilated or markedly dilatable in cases of the profounder grades, and edema of the extremities is common in severe cases of chlorosis and invariably present in advanced terminal leukemia and pernicious anemia. The pulse is usually of low tension and in the more extreme cases of the severer types of the disease a systolic pressure of from 60 to 80 mm. Hg. may be present.

ANEMIC MURMURS.—In cases of marked chlorosis, acute posthemorrhagic anemia and in the pernicious type, one may encounter in its most typical form the curious humming *bruit de diable* over the vessels of the neck. In general, the murmurs associated with anemia are systolic in time and maximal in the second pulmonary interspace, except in instances of extreme blood loss and acutely induced extreme blood deficit. Such murmurs are not widely transmitted and are well confined to the pulmonary field. Similar systolic murmurs may be audible over the aortic area and apex.

It is quite possible to understand that the greatly increased rapidity of the blood stream and the sharp reduction in specific gravity and viscosity encountered in anemias of the severe type may be adequate to explain the occurrence of these bruits. Nevertheless it is probable that other factors are contributory in most instances, the most important of these being the loss of tone in the myocardium and the increased rapidity of the heart beat. In the true anemia murmurs any marked improvement in the condition of the blood is accompanied by a change for the better in any *bruits* present. It should be remembered in this connection that systolic murmurs may occur in the pulmonary area in the absence of anemia of a degree sufficient to be considered causative and that in many instances, bruits, assumed primarily to be anemias, persist long after the blood has reached normal. This would indicate that impairment of myocardial tonus in itself may produce murmurs indistinguishable from those properly attributed to anemia.

Therapeutic Suggestions.—In the experience of the author it has been evident that too little attention has been paid to the condition of the myocardium in the treatment of the severer forms of anemia, whether chlorotic, posthemorrhagic, or pernicious.

In all severe forms **rest in bed** primarily constitutes an important and, in many instances, indispensable adjunct to successful therapy. Furthermore, the degree, amount and duration of such rest should be adequate and the resumption of physical and mental activity as deliberate and systematically planned and carried out as circumstances will permit in the individual case.

Chronic Congenital Asthenia.—In the author's experience cases of chronic congenital asthenia (universal visceroptosis) constitute a large majority of the instances of severe chlorosis encountered, and the condition is associated very often with anemia of the pernicious type.

These individuals are peculiarly vulnerable with respect to circulation, digestion, and the nervous system. They are peculiarly dependent upon the maintenance of an adequately high level of nutrition and the establishment of nutritional reserve, and this balance is very easily disturbed.

In this type of case particularly, one is likely to find marked circulatory disturbances both of the apparently functional type and those representing actual myocardial impairment and cardiac dilatation. In them also the subjective symptoms on the circulatory side may be most troublesome.

In these individuals one may find outward symptoms suggesting aortic regurgitation: throbbing peripheral vessels, water-hammer pulse, and capillary pulse. On the other hand the diastolic bruit of the true lesion is absent save in the rarest instances. The author has reported one case of true diastolic aortic murmur occurring in an individual suffering from Addisonian anemia. At the time his erythrocyte count was below 500,000 per cubic millimeter. At autopsy no adequate cause, aside from extreme degeneration of the heart and atonicity of the myocardium and vessels, was demonstrable.

Nervous System.—A man or woman may suffer from the most extreme forms of anemia and die as the result of them without showing any decided nervous symptoms. On the other hand cases showing relatively moderate degrees of anemia may present almost every symptom known in connection with a disturbed nervous system. Drowsiness, vertigo, extreme irritability, perverted sensations, insomnia, mental depression, hysteria, neuralgia, headaches of all grades even to those so severe as to simulate meningitis, are sometimes common to anemia of all types. Delirium is seldom seen except in terminal pernicious anemia or the last stage of leukemia. The extreme headaches of the pseudomeningitic type occasionally reported in severe chlorosis are rare but extremely troublesome when present. They must be controlled usually by symptomatic treatment and the tendency disappears only when, under the administration of iron in heroic doses, the blood has reached higher levels.

A Cause of Divorce.—The author has been impressed by the almost universal neglect of the lesser grades of chronic secondary anemia such as may be related to chronically infected tonsils, abscessed teeth and like conditions.

A great number of women, especially, go through life with a deficit of from 30 to 40 per cent. of hemoglobin with or without a corresponding reduction in the erythrocytes, and in consequence fail at all times to enjoy health or to carry a normally functioning nervous system. The result in many instances is a chronic irritability of disposition and temperament which is a fertile source of family disagreements and misunderstandings.

Gastro-intestinal Tract.—In chlorosis, the pernicious types of anemia, and in the leukemias one encounters with considerable constancy symptoms referable to disturbed digestion, gastric or intestinal. In some instances these assume forms of great severity and are capable of seriously impairing nutrition. Anorexia, nausea, bulimia, flatulence, vomiting, constipation and diarrhea are the common manifestations.

Terminal Addisonian anemia is often associated with exhausting diarrheal attacks and intercurrent vomiting usually difficult to control and, of course, hastening a fatal issue. In the same cases paroxysmal abdominal pain occurs in about 50 per cent. of the patients and constitutes oftentimes one of the most troublesome sources of complaint.

General Nutrition.—In simple anemia and in chlorosis the superficial fat is usually well preserved, giving the patient a misleading appearance of health in some instances, especially if they belong to the ruddy group of anemics.

In secondary anemia the state of nutrition is dependent upon the primary lesion.

In pernicious anemia, even in its later stages, there exists oftentimes a wholly misleading appearance of fairly good nutrition due to the presence of overlying fat; but the extreme pallor of the mucous membranes, the peculiar color of the skin, its velvety feel, and, in most instances, the jelly-like consistency of the muscles should render any mistake impossible even in the absence of a blood count.

The Eye.—Retinal hemorrhage occurs with some frequency in pernicious anemia, and in all severe forms of anemia the ophthalmoscope shows a pale fundus. Muscular insufficiencies are said to be common but, in the personal experience of the author, have been extremely rare.

THE ANEMIAS

Hemolysis and Regeneration.—The life cycle of the cellular elements of the blood (red and white) and the exact mechanism of their orderly disintegration and replacement still remains a mystery. In health there is little or no variation in the number of erythrocytes or leukocytes from day to day save that the latter transiently vary somewhat with the stages of digestion and the influence exerted by exercise and hot and cold baths.

Active pathologic blood destruction (hemolysis) results always in the release of toxic products and the production of symptoms referable to their presence, but such destruction as occurs in health is unattended by any such phenomena.

The process of erythrocytic hemoglobin retention is itself unknown and to purely physical destructive methods the cell substance offers an absolute resistance to hemoglobin loss, even the most minute shreds and particles of a destroyed erythrocyte retaining their color intact.

The resistance of the red cell to certain chemical agents, on the other hand, is very feeble. "Cell fragility" tests have a certain definite clinical value and the fact that the normal erythrocyte yields its hemoglobin under the influence of a hypotonic sodium chlorid solution of a concentration of from 0.42 to 0.28 per cent. establishes a normal standard of fragility. The higher concentration represents that degree which causes no laking, *i. e.*, hemoglobin loss and diffusion in normal blood; the lower constitutes the degree of dilution of the hypotonic solution which brings about complete hemoglobin loss. Obviously the normal cells vary in their degree of resistance, but within these normal limits only. In "congenital hemolytic jaundice" the fragility of the cell so tested is much greater; in pernicious Addisonian anemia it is less. The terms, "maximum resistance," "minimum breadth" used in connection with such a test, are self-explanatory.

It is plain that erythrocytes are peculiarly susceptible to changes in the blood-plasma salt content. Too great a concentration would shrink and shrivel them; too high a dilution would rob them of their hemoglobin content. Despite this fact, however, "laking" never occurs in the circulating blood and enormous quantities of distilled water introduced intravenously would be required to produce an hemoglobinemia.

Many chemical substances are extremely hemolytic in action (saponin, bile salts, ammonia salts) as are the toxins of many bacteria of the malaria organism, certain snake venoms and the like, but this fact throws little or no light upon the normal life and death cycles of the erythrocyte.

The duration of the life of the red cell in the living human being is "estimated" or "asserted" to be from seven to thirty days. The latter figure has the support of some more or less substantiated proof obtained by following by an ingenious method the fate of erythrocytes introduced by transfusion. This would indicate that through the working of a process wholly unknown a complete removal and replacement, systematic and orderly in character, occurs each month during the lifetime of the individual.

The aged and infirm or injured cells pass probably to the spleen, bone marrow, and liver and are there destroyed by the large mononuclear phagocytic cells ("macrophages") in such a manner as not to expose vulnerable tissue cells to the deleterious effects which would result from any wholesale disintegration within the circulating blood.

The hemoglobin becomes converted into hemosiderin within the splenic, hepatic, and marrow tissues and probably is rendered available for use in the formation of new red cells in the erythrogenetic tissues.

PATHOLOGIC HEMOLYSIS.—In certain diseases and under the influence of toxic agents, known or unknown, wholesale erythrocyte destruction may and does occur together with lysis of blood-platelets and megakaryocytes. This varies widely in degree as does the regenerative activity which must attend or follow it if the hemogenetic tissues are capable of response, *i. e.*, neither inhibited nor aplastic. In some instances, as in severe purpuras, the platelet destruction and consequent shortage is peculiarly marked.

THE BLOOD-PICTURE IN HEMOLYSIS.—In active pathologic hemolysis such as occurs typically in "Addisonian pernicious anemia" the evidences of destruction of the erythrocytes are seen both in the excessive pigment formation, due supposedly to the release of excessive quantities of hemoglobin, in the great reduction of the total erythrocytes, and in the presence of many small deformed red cells.

In addition there may be much cell fragmentation due, it is assumed, to the destruction of megakaryocytes, together with the presence of the bare nuclei of erythroblasts from the bone marrow. In such a case the urobilin and urobilinogen content of the feces and urine is increased greatly and a yellow tint appears in the skin and scleræ of the patient, and bilirubin may appear in excess in the blood-plasma.

It is probable that in such cases the jaundice produced is not purely hematogenous, for the bile capillaries tend to become obstructed and a mild obstructive jaundice plays its part. Such a jaundice is always intensified during the blood crises of an hemolytic anemia of severity and long standing.

Fever, usually of the intermittent type, is the almost invariable accompaniment of active and excessive hemolysis. The tendency to an excessive deposit of iron in certain tissues in hemolytic anemias is well known and this is particularly well marked in the liver and kidneys.

Hemoglobinemia or even hemoglobinuria does not occur in Addisonian pernicious anemia save in rare instances, despite the high degree of hemolysis present. In paroxysmal hemoglobinuria, however, the circulating blood as well as the urine may contain this substance. Cells showing siderosis may occur in the urinary sediment.

BLOOD REGENERATION IN HEMOLYTIC ANEMIAS.—The evidences of hemolysis embodied in the presence of those immature cells indicative of forced and excessive regeneration are more striking than the proofs of blood destruction *per se* furnished by the blood-picture. Nature's reparative reactions are excessive oftentimes and such is the case in hemolytic anemias of a severe type in their active stages. The blood formation in such cases is abnormal in type and excessive along its irregular lines of activity even when a stage of relative futility in results is attained. In such cases the normal fat of the bone marrow undergoes destruction and there is a replacement by hyperplastic tissue and, in certain instances, the liver and spleen may reassume that activity in erythropoiesis normal to them in embryonic life.

The erythroblasts are present in excessive numbers, destruction of erythrocytes by the phagocytic cells is evident, and the platelets and their parent cell, the megakaryocyte, appear in diminished numbers. Hematoblasts may be plentiful and the megaloblasts are present in large numbers.

Blood-picture in Severe Hemolytic Anemia.—The stained blood specimen will reflect the activities of the marrow as set forth in the preceding paragraphs. The red cells are reduced greatly in number but the individual cells are relatively rich in hemoglobin, *i. e.*, the low blood count is not paralleled by the hemoglobin deficit per cell.

There is a great variation in the size of the red blood-cells and the larger forms (macrocytes) predominate amongst the abnormally sized forms. Many cells showing a peculiarly deep staining appear, and large oval cells are peculiarly characteristic of Addisonian pernicious anemia though absent usually in other hemolytic blood conditions. Most peculiar and oftentimes extreme cell deformity is present and the pear-shaped, goblet-formed, and tailed cells may appear in great numbers, together with fragmented cells. Some of the cells present are so small as to be termed microcytes. Reticulated erythrocytes may appear in excessive numbers (10 or even 15 per cent.) when regeneration is active. Nucleated cells appear, megaloblasts, normoblasts, microblasts and even naked cell nuclei. Of these the more immature megaloblast is the most significant and most numerous usually of the nucleated forms present in Addisonian pernicious anemia. In this form of hemolytic anemia especially, "blast" crises appear from time to time, during which their numbers are increased greatly, sometimes to an extent paralleling myelogenous leukemia. In such instances the younger (reticulated) forms of the non-nucleated red cells may be increased very greatly.

White cell production in the marrow is inhibited to a greater or less degree and a leukopenia results. The appearance of myelocytes in considerable numbers may be interpreted as indicating excessive regenerative effort on the part of the marrow. Relative lymphocytosis, the result of deficiency in the polymorphonuclear cells, is a not infrequent finding.

It will be observed that the elements of the blood-picture especially indicative of excessive regenerative action are such immature forms as the polychromatophilic red cells, the normoblasts, megaloblasts and the reticulated cells, if these last appear in excessive numbers. In certain anemias the opposite condition governs and there is little or no evidence of hyperplastic activity or even a mild regenerative process. This is typified in the idiopathic pernicious aplastic anemia.

In hemolytic anemias of moderate grade only a secondary anemia may be present of the usual type lacking any striking evidence of the blood destruction or of excessive regenerative activity.

The Origin and Destruction of the Leukocytes.—The white cells of the blood originate not alone in the lymphadenoid tissues but in the bone marrow as well, and all of the granule-bearing leukocytes come from the myelocytes of the marrow and these in turn from the myeloblasts springing from the same tissue.

The lymphocytes arise from small round cells (lymphoblasts) present in the follicles of the lymph glands, the malpighian bodies of the spleen, the intestine, thymus, etc., and are themselves indistinguishable from the parent cell.

The myeloblasts of the bone marrow when present in the circulating blood are distinguishable from the large lymphocyte and the lymphoblast of lymphadenoid tissue only by special staining methods.

Destruction of the Granular Leukocytes.—The mode of disposition and the life cycle of these cells is unknown. There is,of course,a constant tendency towards migration outside the vessel walls and many are disposed of through the respiratory channels, intestines, the tonsils, and the mucous membranes in general.

The leukocytes are rich in protease and peculiarly susceptible to autolysis which readily becomes excessive if anything operates to abate the influence of the antienzymes present in the circulating blood. In all probability the greater destruction in health takes place in the spleen and other organs. The disturbance resulting from pathologic leukocyte disintegration is much less than that which accompanies the wholesale destruction of red cells. The fate of the lymphocyte is unknown.

CHLOROSIS

Definition.—Chlorosis is a disease of unknown specific causation but supposed to be due to defective blood formation. It is characterized by a pronounced anemia, the outstanding clinical characteristic of which is the hemoglobin deficit (the erythrocyte count being but slightly affected in primary attacks), and the astonishing response shown by the disease to the internal administration of iron.

Etiology.—Although this disease has been known and recognized since, and before, the days of Hippocrates, its specific fundamental etiology is not known. It may be stated, however, with positiveness that its onset is associated with peculiar constancy with the period of sexual development in the female and one may assume, therefore, that the blood changes result from some fault of function in the glands of internal secretion. It would appear certain that its incidence in our own country has decreased strikingly during the past twenty years—a period characterized by greatly improved living conditions, a better understanding of concealed septic foci, and the free exhibition of Blaud's mass and other preparations of iron in the "department" stores.

AGE AND SEX.—Although a few cases of anemia of the chlorotic type have been described as occurring in young males, its incidence, nevertheless, is almost exclusively limited to the female sex and, so far as primary attacks are concerned, 99 per cent. of these occur between the ages of 14 and 25, and by far the larger proportion between the fourteenth and eighteenth years. Obviously this latter period corresponds suggestively to that immediately preceding, accompanying, or following the establishment of menstruation. It represents also the age of maximal susceptibility to focal infections. Inasmuch as the disease shows a peculiar tendency to chronicity and recurrence under the usual casual and unsystematic management on the part of patient and physician alike, one encounters frequently cases of chronic or recurrent anemia of the chlorotic type at later ages and occasionally even in middle age.

THE CONGENITAL ASTHENIC.—According to the author's experience nearly all of the cases of pronounced chlorosis occur in individuals of the congenitally asthenic (universally visceroptotic) type. The characteristics of this peculiar type of constitutional inadequacy or inferiority are such as would favor or predispose to the development of chlorosis, whether this be considered as fundamentally the result of disturbance of endocrine function, nutritional deficit, or the result of infections.

In these congenitally asthenic individuals there is a peculiar nutritional instability and an unfortunate dependence upon nutritional reserve for the maintenance of health and normal function. The larger number of cases of endocrine disturbance, of gastric neurosis, of cardiovascular abnormalities of the functional type, are associated with the presence of the "drop heart," abdominal visceroptosis, a narrow costal angle and the slender bony and muscular structure characteristic of this type.

In these congenital asthenics, particularly, one finds with especial frequency not only focal infections of the usual type but radiographic evidence of larval or obsolete tuberculosis of pulmonary site. It has long been known that this is true also of cases of chlorosis.

The readiness with which disturbance of function occurs in connection with this constitutional state makes it easy to understand that deficient bone-marrow activity might occur readily in connection with it and indeed both the symptomatology and the etiologic indications accord with the assumption that in the greater number of instances one is dealing with this peculiarly vulnerable and unstable type.

OLDER THEORIES OF CAUSATION.—Among the numerous and diverse theories which have been advanced in the past, one may note the following:

(*a*) Lovesickness is given as a cause. Of course, this may be and often is encountered in a disease affecting almost exclusively young girls and young women of the age which peculiarly predisposes to this state of mind and body.

(*b*) Hypoplasia of the generative organs has also been advanced as a cause and is present no doubt in a certain proportion of the chlorotic cases. However,it would be improper in the light of present knowledge to consider this in itself a direct cause or a constant associated etiologic factor.

(*c*) Tuberculosis, cardiovascular defects, heredity, psychoneurasthenic states, constipation and autointoxication, for the most part represent effects rather than causes and defects peculiarly likely to be encountered in connection with the congenitally asthenic type.

(*d*) Overwork, bad food, unhygienic environment, worry and mental depression, and even certain specific occupations have been advanced as causative factors. Doubtless each and every one may be considered a potential contributory element, but certainly no one of them can be put down as a specific factor in etiology.

(*e*) Much stress has been laid by certain writers upon the potency of homesickness as a factor in chlorosis and it is quite true that one encounters a large number of chlorotics amongst the recently arrived immigrants, especially such as come from northern countries as those of Scandinavia. Usually, however, it is unlikely that homesickness plays a part more important in itself than any other state of mental depression and worry; and furthermore, in the class of individuals just mentioned, many other factors favorable to the development of the chlorotic state are present. The larger number of these young female immigrants have come from the farms, from an open country life with coarse wholesome food and abundance of outdoor work, and have exchanged these favorable conditions of environment for city living, domestic service, work in public laundries, and other occupations of a relatively unfavorable nature.

(*f*) There can be little doubt that chronic concealed septic foci may play a part in the production and more especially in the persistence and recurrence of chlorosis, yet the greater number of anemias for which chronic infections of the tonsils, teeth, and other organs are responsible are of the secondary type to be described later and not of the chlorotic type.

Unfavorable Environment.—The betterment of conditions of living and working has undoubtedly resulted in a marked diminution in the incidence of cases of chlorosis as might be expected when one considers the large number of contributory factors in etiology involved in bad housing, whether related to dwellings or shops, insufficient and improperly prepared food, excessively long working hours with resulting tendency to extreme fatigue and deprivation of fresh air and sunshine for the indoor dweller or worker. Each and every one of these factors is of vital importance to health in general and especially to the maintenance of good health on the part of those of the congenitally asthenic type of constitution.

Symptomatology.—Clinical History.—The onset is gradual, usually extending over a period of several months, but in rare instances the disease develops somewhat acutely. Few diseases give rise to a greater number and variety of symptoms than does chlorosis. Practically every function of the body of the victim may be impaired and one or a number of these may seek to express their disability in terms of clinical symptoms of varying grade and character.

The disease usually has reached a somewhat pronounced stage before any symptoms are noted on the part of the patient, the family or the physician, and as a result by far the greater number of chlorotics present a striking clinical picture when seen first by the physician.

The history of the patient reveals almost always the presence of certain of the contributory etiologic factors discussed in preceding paragraphs. One seldom encounters chlorosis in country girls well-fed and leading an open-air life, and it must be remembered that, even though the greater number of cases occurring in crowded centers of population arise amongst the poor, a considerable number occur amongst the well-to-do classes as well.

If living conditions with respect to sunshine, fresh air, healthful exercise, proper food, adequate sleep and the like are defective or absent, the young girl or woman living at a fashionable boarding school with millions behind her has no greater protection than the daughter of working people, herself employed in a laundry or kitchen. Indeed, poorly conducted boarding schools are prolific sources of cases of chlorosis. In any event it is necessary to carefully check and oftentimes to cross-examine the patient with reference to living and working conditions.

Subjective Symptoms.—One of the earliest symptoms complained of usually is *loss of energy,* and with this goes unusual fatigability. *Disturbances of sleep* are extremely common and are peculiarly inconstant in that one patient may complain of insomnia or bad dreams and interrupted sleep, whereas another may be troubled by drowsiness particularly during the waking hours.

Nervous irritability, as might be expected, is extremely common, is often misunderstood and, in many instances where the ailment is unrecognized by friends and parents, leads to most unjust punishment and false estimates of character. It is quite impossible for the young growing and developing girl, with a hemoglobin percentage of 30, 40 or 50 only, to be quite normal with respect to her cerebral functions and much allowance must be made.

Headache is a common symptom and in certain rare instances, only three of which have occurred in patients of the author, may assume so severe a form as to simulate an actual meningitis. In the greater number of instances these chlorotic headaches are relatively mild but may be most troublesome in their persistence or the frequency of their recurrence.

Another symptom which may prove very troublesome is *deficient mental application* leading to poor scholarship and, as in the case of irritability, to unjust punishments and harsh disciplinary measures.

The Gastro-intestinal Tract.—The gastro-intestinal disturbances of chlorosis are chiefly those falling under the head of the gastro-intestinal neuroses, separately and fully described elsewhere in this work. Capriciousness of appetite and sometimes marked abnormalities associated with craving for unusual or even disgusting articles, together with flatulence, heartburn, vague and often shifting and irregular epigastric distress after meals, hunger-pain, and the like are some of the prominent features.

Gastric ulcer is peculiarly frequent in chlorotics and consequently one should not hold too lightly symptoms which might readily be interpreted as purely nervous. In all such cases a careful anamnesis and physical examination are indispensable if serious error is to be avoided.

Constipation.—Constipation is a troublesome and relatively constant symptom in this ailment and this fact has given rise to the theory of autointoxication as the primary fundamental and etiologic factor, an assumption which is not justified and presumably is no longer widely held or affirmed.

Disturbances of Menstruation.—Bearing in mind the age at which the manifestations of chlorosis appear, the marked nutritional disturbances which accompany it, and the apparent association of the disease with the development of the sexual organs, it will be understood readily that disturbances of menstruation are extremely frequent. These may take the form of postponed appearance of the periods, dysmenorrhea, menorrhagia, or, more often, deficiency and irregularity in the flow.

Cardiovascular System.—In individuals of the congenitally asthenic type there is a peculiar circulatory lability associated with a "drop heart" which, like the other organs of the body possessing a special function, is peculiarly sensitive to nutritional defects and endocrine disturbances, one or both of which may play an important part in the development and course of a case of chlorosis. If one adds to these factors that of excessive instability and irritability of the cerebrospinal system and a known deficiency in the oxygenation of the blood associated with a greatly increased rapidity of the blood stream, he is in a position to understand how readily troublesome and impressive disturbances of the circulatory system may arise in these cases.

Furthermore, it should be understood more generally and clearly than at present that the cardiovascular disturbances associated with chlorosis are not of necessity purely functional.

Arhythmias are common and usually of the simpler forms; tachycardia is a common symptom and may be more or less persistent or most troublesomely recurrent; dyspnea on exertion is an almost invariable symptom in any marked case of chlorosis and may be attributable either to the condition of the blood alone or to an accompanying myocardial insufficiency with or without actual dilatation of the heart.

Edema of the ankles and, less frequently, puffiness of the face are clinical signs of importance frequently present in the more marked grades of chlorosis.

In the past it seems to have been the rule to regard the gravity edema as a symptom attributable to the blood condition. Any one, however, who has systematically x-rayed the hearts of these patients on the basis of an interpretive appreciation of the possibilities of the drop heart with relation to dilatation and myocardial insufficiency, and who has seen the dependent edema disappear under rest in bed and cardiac stimulation long before the administration of effective doses of iron could produce an effect, must believe as the author does that these symptoms are due to circulatory inadequacy and not primarily or chiefly to the blood condition itself.

Physical Findings.—*Outward Signs.*—The most striking outward symptom of chlorosis is found usually in the color of the patient's skin and mucous membranes. In the case of the former, one may be misled very easily by the presence of a rosy color in the cheeks and a vivid red in the lips in instances of the so-called "rosy chlorotics." So far as the author's observation has gone, these rosy chlorotics, so-called, represent nothing but cases of weak right heart or defective mitral valve, functional or organic in nature, but it is interesting to note how good a presentment of robust and ruddy health may be encountered in some of these patients. When, however, one examines the pharynx, the gums, and more particularly the ocular conjunctivæ he is very quickly undeceived and the anemia is very definitely established.

In certain instances the skin and especially the face is not only pallid but shows a greenish-yellow tint which has given the disease its name (green sickness). By far the larger number of chlorotic patients show simple pallor, however, and not this peculiar coloring, so that the name "chlorosis" must be considered in a measure a misnomer in these days of prompter and more accurate diagnosis.

Puffiness of the face is not uncommon, as stated, and a certain amount of hydremia is accountable no doubt for its presence. Indeed we know at the present day that to a considerable degree this condition exists in cases of chlorosis, presumptively largely as a result of cardiovascular impairment secondary to the anemia and general nutritional disturbance.

Superficial Fat.—In most of the cases of chlorotic anemia the superficial fat is rather well-preserved, sometimes to a misleading extent, and indeed the same statement is applicable to the severe, fatal, progressive and pernicious type of anemia to be described later under the name of Addison, its discoverer. Deficient oxidation no doubt is responsible in large measure for this peculiarity.

Dyspnea on Exertion.—An effort dyspnea may be noticeable in these patients either as a direct result of exercise or effort taken at the request of the physician and as a part of the examination, or occurring merely as the result of excitement. The underlying cause may be purely a blood impairment and oxygen deficiency or, as is more commonly the case in any severe anemia, represents a combination of myocardial weakness and hemoglobin deficit. It is a symptom common to all severe types of anemia, acute or chronic. Further observation and examination of the patient may reveal edema of the ankles, evidence of disturbed heart function in the shape of arhythmias, the presence of the so-called anemic murmurs or an actual cardiac dilatation.

Most bizzare symptoms of an hysterical or psychasthenic type may manifest themselves during the physical examination and in some instances the mental status and outward appearance of the patient may give rise to serious questions with respect to the presence or absence of a true psychosis.

Warning.—Chlorosis is one of the diseases peculiarly likely to mislead the unwary student or physician into the error of so concentrating his attention upon the striking symptoms of this disease as to overlook other and perhaps more serious conditions of which it may be only a part or an accidental concurrence. Particular care should be taken with respect to the presence or absence of an active tuberculosis in these cases and, as stated heretofore, to the determination of the presence or absence of a gastric ulcer in cases where gastro-intestinal symptoms are decided.

LABORATORY FINDINGS AND SPECIAL EXAMINATION.—*The Blood.*—The outstanding feature with respect to the blood findings in chlorosis is the decided poverty of the individual erythrocyte in hemoglobin. The blood appears pale macroscopically, is thin, and the specific gravity, of course, is low. The hemoglobin percentage will be found to vary widely in the different cases (from 12 to 75 per cent.) averaging about 45 per cent. in any large group of observed chlorotics.

The red cells are not decreased proportionately, the average being about 4,000,000 per cubic millimeter. An erythrocyte count under 2,000,000 is rare and occurs apparently only in cases of long standing which have taken on some of the aspects of a severe secondary anemia. The average size of the erythrocyte as seen in the microscopic field is less than normal, a matter of some diagnostic importance.

Stained specimens show more or less marked achromia and old cases may show slight and, more rarely, marked variation in the size of the cells (anisocytosis) and a trifling degree of polychromasia. Any decided cell deformity (poikilocytosis) is very rare and never extreme, but may be observed in certain recurrent cases of unusual chronicity and severity.

Reticulated red cells are not increased. Nucleated red cells are seldom found and when present are normoblasts. The blood-platelets are markedly increased. Myelocytes are found but rarely; the eosinophils are decreased, and the "coagulation time" is short.

With regard to the number of leukocytes, the testimony of different observers is conflicting. According to the author's experience they have been for the most part about normal. Osler reports a series of cases in which the average count is somewhat high, averaging 8,467 per cubic millimeter; Gulland and Goodall, a series in which the white cell average fell under 5,000. In the old, long-standing cases a leukopenia may be present and in rare instances there is a lymphocytosis.

The total amount of the blood is now assumed to be increased in these cases, though the grounds for this assumption are somewhat unstable, and, as stated heretofore, in those of a more advanced type with poor circulation a certain amount of hydremia is present.

Diagnosis.—Manifestly primary attacks of chlorosis may be diagnosticated easily, and diagnosis will be based upon the following factors:

1. *Indirect.*—The age of the patient; the history of onset; the appearance of the skin and mucous membranes.

2. *Direct.*—The striking achromia of the erythrocytes, as seen in the stained or even unstained specimen under the microscope, so varies with the degree of hemoglobin deficit as to enable an expert laboratory man to estimate roughly the hemoglobin percentage.

To this one adds as a direct confirmatory factor the relatively slight or the moderate reduction in the red blood-cells and the consequent low "color index." As a matter of fact there is little excuse for failing to make a diagnosis of chlorosis if a man has a microscope and the ability to use it even in connection with the simplest of laboratory technic. In a very large proportion of the cases, moreover, a diagnosis might be quite accurately made without recourse to the microscope, particularly if final judgment were held in abeyance until the patient had been under proper conditions of treatment for a short time. The remarkable effect of the administration of iron under proper conditions and in adequate doses is so striking as to form properly a part of the diagnostic structure.

In cases of chlorosis of the extremely chronic severe recurrent type the diagnostic picture is less clearly defined but seldom so far modified as to justify a mistaken opinion.

Great variations in form and striking abnormalities of outline do not occur and the prevalent type of cell remains small, the color index low, the appearance of the stained or unstained erythrocyte clearly indicating that the anemia is chiefly the result of hemoglobin deficit, and if blasts are present they are of the small normoblastic type and unlikely to lead to error.

In pernicious anemia the hemoglobin value of the erythrocyte is high and the erythrocyte count shows marked reduction as the most outstanding features of that disease.

In the Addisonian type of pernicious anemia one finds ordinarily the predominance of the larger type of erythrocytes and the presence also of megaloblasts. If nucleated cells are present in chlorosis they are normoblasts in nearly every instance.

In the chronic form of chlorosis or the chronic recurrent type, as has been stated previously, one may find slight variation in the size of the erythrocyte (anisocytosis), some polychromasia, very rarely a certain amount of cell deformity (poikilocytosis), and sometimes a considerable reduction in the number of erythrocytes per cubic millimeter.

This picture, however, need not confuse any one with respect to a mistaken diagnosis of pernicious anemia inasmuch as the picture is distinctly one approaching the secondary type in which ordinarily there exists a relative or approximate equality in the erythrocyte and hemoglobin deficit in the blood.

One need not waste time, therefore, upon any elaborate discussion of differentiation. There is practically no likeness between the usual form of chlorosis and pernicious anemia and only the faintest resemblance between the two diseases in the case of chronic or chronically recurring chlorosis.

The differential diagnosis of leukemia needs no discussion here as the blood-picture is wholly different from that of chlorosis.

Anemia from Malignant Disease.—In general the anemia of malignant disease is distinctly of the secondary type in which there is an approximate equality in the hemoglobin and erythrocyte deficiency. In some instances, however, the blood-picture resembles that of chlorosis in the earlier stages of the malignant process and this fact should be borne in mind as a possibility and is one of the many reasons for an accurate thorough-going examination of all anemic individuals.

In certain advanced cases of malignant growth and especially such as involve the stomach and of rapid progression and hepatic metastases, one meets with an anemia which may suggest chlorosis but quite as often is misleadingly like pernicious anemia in that a very great reduction of the erythrocytes may occur and the hemoglobin value of the individual cell be high. In such cases, however, there is in actual practice little liability of serious error as regards the making of an erroneous diagnosis of chlorosis. The error, when made, usually consists in interpreting the blood findings in such a case of malignancy as indicating an Addisonian pernicious anemia.

The cases, so far as the author's experience goes, lack the dominance of the large erythrocyte forms and the megaloblast and seldom show so high a color index as does pernicious anemia. Furthermore, in cases capable of producing a secondary anemia of so high a grade the clinical signs of malignancy usually are obtrusive and not likely to be overlooked.

THE ANEMIAS OF TUBERCULOSIS.—In the earlier stages of tuberculosis an anemia may appear which cannot be differentiated from chlorosis and as a matter of fact the type of individual most frequently encountered in chlorosis is peculiarly predisposed to tuberculosis. In the later stages of tuberculous infection the anemia takes on the characteristics of the secondary type. In this connection one need only point out again the urgent need of careful and thorough examinations in these cases.

POSTHEMORRHAGIC ANEMIAS.—The anemias due to hemorrhage, whether acute, subacute or recurrent, massive or incremental, ordinarily take the form of the secondary type of anemia. In all cases, however, questions should be asked and any necessary examinations made to exclude chronic, repeated, or merely recent hemorrhage as a fundamental or contributory cause of any existing anemia.

THE ANEMIA OF RENAL DISEASE.—In any form of nephritis, acute or chronic, there may be anemia and this is most marked in the acute Bright's disease and the chronic parenchymatous nephritis. The production of anemia in the case of acute Bright's is understood readily when we consider the blood loss which occurs through the urine in that disease and, furthermore, the fact that the disease itself is in most instances the sequence of an acute infection.

In chronic parenchymatous nephritis there is a persistent impairment of metabolism and nutrition, a constant albuminous output and oftentimes recurring hemorrhages. This latter type of case shows great variations in the degree of anemia present. In some instances it is so marked and severe as to suggest pernicious anemia; in others it is merely a moderate and apparently trivial secondary anemia in grade.

THE ANEMIAS DUE TO INFECTIONS.—The fact that most of the infectious diseases are associated with the development of anemia must be borne in mind no less than the fact that great variation exists in the degree to which this change in the blood may be induced by the various pathologic microörganisms. It must also be borne in mind that the chronic infections, and particularly those represented by concealed septic foci, are potent factors in the production of secondary anemia and play a part also in many cases of chlorosis.

Complications and Sequelæ.—By far the most serious complication of chlorosis is the impermanency of cure so frequently encountered as a result either of lack of persistency on the part of the physician or oftener because of failure on the part of the patient to carry out instructions or, perhaps to go to the physician at all. A great many cases of chronic anemia carried through life to the great detriment of the individual are brought about in this way.

GASTRIC ULCER.—The frequency of gastric ulcer in connection with chlorosis has long been noted and many writers have given to this form of anemia a prominent place amongst the causative factors of that serious gastric ailment.

SINUS AND VENOUS THROMBOSIS.—A special tendency to thromboses of sinuses and of the veins exists in chlorosis, the proportion of occurrence as between the two sites being as 2 to 1. If sinus thrombosis occurs it is usually associated with venous thrombosis elsewhere and the issue is nearly always a fatal one.

MYOCARDIAL INSUFFICIENCY.—A certain amount of myocardial weakness and relative insufficiency must occur in connection with a pronounced and severe anemia of any type, chlorosis being no exception. Furthermore, in many instances there exists an actual dilatation of the heart and secondary edema of the cardiac type. Many of the symptoms so readily attributed to the blood condition are actually cardiac in origin, representing a loss of myocardial reserve due to toxemia, deficient blood supply, and the resulting tonus impairment. In cases where exertion dyspnea with or without edema has been present in marked degree, one will note usually that these symptoms do not disappear *pari passu* with the improvement of the blood condition, the myocardial insufficiency being relatively laggard as might be expected.

Treatment.—It is unfortunate perhaps that the medical profession and the laity alike so thoroughly understand the response of chlorotic anemia to iron that the treatment of the disease has been made to appear so simple that a vast amount of neglect and imperfect therapy result.

Every department store sells Blaud's mass or other preparations containing iron; every one knows that iron is a tonic and is good for the blood; and every doctor has at his fingers' end various iron-containing prescriptions which are curative if properly applied in cases of chlorosis. As the result of these apparently fortunate circumstances there is a tendency to misunderstand certain traits in this disease, especially such as relate to recurrence and chronicity.

In all severe cases of chlorosis, moreover, **physical rest** should be combined with the administration of **iron**, and the greatest possible reinforcement of nutrition undertaken with the object of establishing a proper reserve. Cases of chlorotic anemia treated as ambulants are peculiarly likely to recover only partially and, furthermore, take a much longer time to make the necessary improvement.

Cases self-treated and those handled by physicians who do not appreciate the extraordinary tendency to relapse may drift into chronicity and make miserable the life of the patient, sometimes also the lives of those around them.

GENERAL FACTORS IN THE THERAPY OF CHLOROSIS.—As has been suggested, the fundamental factors are represented by the maximum of **physical rest** and **mental serenity** obtainable, combined with **adequate** and **suitable feeding** and the administration of adequate amounts of **iron** over sufficient periods of time. Physical exertion to the point of actual fatigue should be avoided so far as possible until the patient's health is fully reëstablished. Many cases of relapse result from a neglect of this simple precaution.

As a corollary to this it should be said that no case can be properly handled without subjecting the blood to frequent tests for hemoglobin percentage, for the results of treatment should not be affirmed or predicated upon the sensations of the patient or even improvement in the color of the skin and mucous membranes but the rehabilitation of the individual's blood should be brought squarely up to the normal and there maintained.

SUBORDINATE AND CONTRIBUTORY FACTORS IN TREATMENT.—Under the heading of etiology a large number of more or less minor factors have been considered and to each of these should be given a place and a certain value in connection with treatment. Most careful inquiry should be directed and oftentimes a careful or tactful cross-examination conducted which will bring out as clearly as may be all of the deleterious factors entering into the production of the disease in the individual under examination.

The **diet** must be most carefully looked into and one must be certain that any deficiency therein is corrected so far as possible. This involves in not a few instances an attempt to correct the ideas of the individual patient with respect to the articles of food which properly enter into a nourishing dietary.

With respect to the nature of the foodstuffs, one need say little. Meat, vegetables, sweets, all have their place and so far as possible some balance and proper proportion should be maintained. Eggs, spinach, oatmeal, butter, cream, and above all, red meats are the most useful.

In the case of most individuals, and particularly those treated as nearly all should be primarily, in **bed**, it is well to place them upon not less than **six feedings a day** and to make the dietary as nourishing and simple as possible, having due regard to the tastes and unavoidable idiosyncrasies of the patient.

One frequently encounters an apparent idiosyncrasy with respect to certain articles of food and this should receive due attention and be treated with proper respect. On the other hand one finds chlorotics especially demanding at times unusual articles of diet and possessing for these a special craving. This is particularly true of substances containing acids, such as pickles, olives and the like, but the same craving may be manifested for sweets or even more or less bizarre articles such as smoked herring, cooked or uncooked; and here again one should be willing usually to meet the patient's craving with reasonable and rational indulgence.

Where this longing exists in the patient, it will be found oftentimes that it may be satisfied without harm and sometimes with great benefit and, furthermore, that even in cases of markedly disturbed digestion articles of food craved by the patient which are distinctly contra-indicated according to dietetic rules may be eaten and digested without harmful effect of any kind. Certain very striking instances of this sort have occurred in the practice of the author.

This does not mean necessarily that the articles desired represent any distinct legitimate demand on the part of the body tissues, although in some instances this is the case, but it is certain that by indulging such whims one may often obtain from the patient a willingness to be nourished to a degree impossible if he or she is denied.

All food should be tastefully served and seasoned while cooking, and too great uniformity and monotony in the meals should be avoided. There is no reason why coffee should be bad, but tea ought not to be taken when iron is being administered. Milk is valuable in the dietary but is best taken as bread-and-milk, crackers-and-milk, or in connection with cereals. Many patients cannot take raw milk without suffering from flatulence and indigestion unless it is combined with other solid substance as is suggested here.

Hyperacidity is a very common symptom in chlorosis and is best treated with milk of magnesia, bismuth subcarbonate, sodium bicarbonate, and proper modification of the diet.

FLATULENCE IN THE ANEMIAS.—In the case of all patients with digestive disturbances, particularly with any tendency to flatulence, a limitation of fluid intake oftentimes is of prime importance and this is a matter which is usually wholly overlooked by the practitioner. When the digestion is disturbed it is the common habit to prescribe a liquid diet acting upon the theory that this offers the least resistance to digestion and hence is indicated. As a matter of fact it is often most unwise, and the cutting out of liquids and substitution of simple, **thoroughly cooked solids** will correct troublesome or even serious cases of flatulence distress. The foregoing statement is especially applicable to patients kept in bed, whatever the nature of their trouble.

Another error occasionally made consists in the overfrequent and untimely and illy-regulated giving of fruits. As has been stated elsewhere, the best time to take fruit is before breakfast and in general the early part of the day; the worst time, after five o'clock in the afternoon. The difference between the raw fruit and cooked fruit is probably much less with respect to disturbances of digestion than is supposed, and one will do well to include both varieties in the same category and treat them in the same way.

Furthermore, one should bear in mind that the excessive ingestion of citrous fruits may produce a troublesome spastic constipation. The author has encountered instances of this condition due wholly to the cause stated and not removable until citrous fruit was wholly withdrawn or radically limited.

CONSTIPATION.—Many cases of anemia are victims of more or less obstinate constipation and this may be intensified in chlorosis or simple anemia especially by the iron demanded in the treatment of the case. Commonly it is sufficient to use any of the **mild laxatives**, either alone or in combination with the other remedies, but in the greater number of instances the use of **fruit** and the **drinking of water** in the early morning hours before food is taken, with a certain amount of instruction given the patient will suffice to relieve the trouble.

It is probable that at least 75 per cent. of the cases of constipation are purely due to lack of understanding of the physiologic process on the part of the patient himself and this statement is true especially of adults and healthy people. In them the rectal reflex may have become so blunted as to render the normal stimulus caused by the descent of fecal matter insufficient to constitute a recognized demand for stool; hence, the value of regularity in going to stool regardless of any demand on the part of the bowel.

In the case of walking patients, furthermore, the importance of assuming a **sharply flexed position** of the **body** so extreme as to bring about the reinforcement of the action of the abdominal muscles by pressure upon the thighs is not understood sufficiently. Not only does this attitude secure the maximum of reinforcement pressure but it seems to produce a relaxation of the sphincter which is most important and valuable.

In addition to these measures, the use of **bran** either as a cereal or incorporated in bran bread or biscuit, the use of **olive oil enemata** at bedtime (4, 6, or 8 ounces [113.4, 170.10, or 226.8 grams]), and, when absolutely necessary, the employment of the ordinary **soapsuds enema**, may be measures of value. In many instances the use of the various preparations of **mineral oil** as a mere mechanical agent works well, but wherever possible constipation should be overcome without recourse to drugs.

In the case of bed patients who have to use the bedpan, it is occasionally absolutely necessary to give laxatives, saline or otherwise, but in some of these instances proper instructions and the use of mere **manual pressure** as reinforcement pressure over the abdomen may correct the difficulties encountered.

FRESH AIR, SUNSHINE AND REGULATED EXERCISE.—If **fresh air** and **sunshine** have been lacking they must be supplied so far as possible and, as the patient improves in strength and well-being and the blood findings justify it, **exercise** should be resumed gradually and systematically and persisted in.

In many instances it is necessary for the physician to enter as closely into the mental status of the individual as is humanly possible and he often must become guide, comforter and friend and seek to do away with certain false modes of thought and reasoning which may, if persisted in, almost wholly negative the effects of rational treatment.

THE ORAL ADMINISTRATION OF IRON.—It is difficult to understand why a shortage of iron should appear in chlorotics, and no adequate explanation so far has appeared. We have really gone no further than a knowledge of the fact that, whereas in health and under a normal dietary the necessities of the bone marrow are supplied properly, yet under conditions developing chlorosis the food content of iron must be reinforced by the administration of the metal in some form, organic or inorganic.

It is interesting to note that in the case of infants who have become anemic under improper feeding, the administration of proper iron-containing food alone is sufficient to cure the anemia and vastly to improve the nutrition of the child.

Inasmuch as iron is the all-important direct therapeutic agent in the treatment of this disease, one may properly devote some space to the best methods of administration and to cautions bearing upon certain common errors in that connection.

There are two chief methods of administration of iron, the commoner one being the use of the gastro-intestinal canal, the medicine being administered in liquid or solid form by mouth. The second consists in the hypodermic administration, or even the introduction of solutions into the veins.

Two classes of preparations of iron are in common use,—(*a*) organic and (*b*) inorganic; but whatever the preparation, conversion takes place in the stomach into ferric chlorid, and inorganic salt.

Many of the special preparations containing organic iron are "elegant" pharmaceutically considered, and some are reasonably effective, but the best results are obtained apparently with some of the simplest and oldest inorganic compounds or iron.

All things considered, the best of these is found to be the **Blaud's mass.** This preparation is not astringent and is usually well tolerated by the stomach. It can and should be obtained of the pharmacist, freshly made and administered preferably in capsules. The mistake is made commonly of giving much too small doses and in failure to push strenuously the administration of the drug. Instead of prescribing Blaud's mass in capsules or pills in the amount of 5 grains (.324 gram) three times a day, a beginning should be made with 10 grains (.650 gram) and 5 grains should be added every second day until the patient is taking about 90 grains (5.85 grams) of the mass daily. Administration is continued on or about this level until the blood becomes normal and the treatment should be carried on if possible over a period of several weeks thereafter in gradually diminishing dosage.

It is usually necessary to give some simple laxative at the same time either as a part of the Blaud's pill itself, or better probably, separately. **Phenolphthalein, aloes, cascara sagrada,** or **sodium phosphate,** or some other simple saline laxative may be used for this purpose. If the appetite is affected, as so often happens, the **tincture of perchlorid of iron** in doses of from 10 to 30 minims (.63 to 1.90 c.c.) may be given, well diluted and in a syrupy vehicle.

In cases where it may be thought that an iodid is indicated the **syrup of the iodid of iron** will prove very valuable and may be given to adults in doses of 15 to 30 minims (.92 to 1.90 c.c.) well diluted.

In administering liquid preparations of iron by mouth the dose should be taken through a glass tube, or, lacking this, the mouth should be thoroughly rinsed out each time. A very large number of preparations of organic iron compounds have been put on the market from time to time and many of these are effective but it may be questioned whether they are any more, or as much so, as the old Blaud's mass.

Several observers have reported their belief that the results of iron administration were improved if an intestinal antiseptic such as **beta-naphthol** or **salol** were given, and in certain cases the author has found that this is true in certain patients of his own.

The appearance of gastric disturbance may, of course, make a modification of this method necessary. If this appears after several days or weeks of successful administration it is better to wholly suspend the use of the iron by the mouth for a few days or a week or two, using **intramuscular injections** twice weekly of a suitable hypodermic preparation, and then recommence on the basis of moderate yet full dosage.

The iron should be continued if possible for as long a period as a rise in hemoglobin can be proven in the blood of the patient. When the hemoglobin percentage has reached 90 the administration of iron should be still continued, if possible, under diminishing dosage as stated above over a period of three or four weeks. The patient should be recalled for another test within a week or two weeks after any cessation of treatment and, whether or not the hemoglobin percentage has remained stationary, the administration of iron should be renewed. In the former instance it will need to be continued only for a few days at a time until the hemoglobin percentage appears to be stabilized at the normal figure.

As in the case of so many other drugs, the continuous administration of iron over long periods causes a loss in its efficacy, hence even in chlorosis where it is the curative drug one does not continue it ordinarily for longer periods than two months, then interrupt its administration for one, two or three weeks, and going on with alternating administration and withdrawal for several months thereafter.

THE HYPODERMIC USE OF IRON.—The administration of iron subcutaneously has become more popular of late and has for its purpose the securing of more rapid action and more complete absorption and assimilation. The citrate of iron and ammonium is the preparation most commonly used but in certain instances gives rise tó considerable pain and irritation.

The following solution of iron and arsenic has proved very successful and free from untoward results connected with administration:

Ferri citratis viridis	0.05 gram (¾ grain).
Sodii arsenatis anhydrous	0.002 gram (1/32 grain).
Aquam	ad 1 c.c.

Burroughs, Wellcome and Company put up this solution under their Hypoloid brand and in the form of ampules, making an extremely convenient form for administration. Administered in this form it should be given two or three times weekly.

If the ferrous ammonium citrate is used, the fact should be borne in mind that the severer the anemia and the more impaired the nutrition of the patient, the more likely is there to be some untoward reaction to the remedy.

ARSENIC.—In certain cases of chronic chlorosis and simple anemia it will be found that **arsenic** clearly increases the potency of iron administration. In such instances it is better to administer **Fowler's solution** or combine a small dose, grain 1/60 (gram .00108) with Blaud's mass.

MANGANESE.—It has also been maintained over a long period that manganese increases the potency of iron and one of the commonest preparations in use is the **liquor ferri peptonati manganesi.** Whether this be true or not, the author can affirm that great benefit is obtained through a change in the preparation of iron administered. Every physician should be in a position to keep track of his supposedly cured cases of chlorosis and should follow them for a period of at least two years if possible.

The author would not be misunderstood as asserting that Blaud's mass is the only drug with which chlorotic anemia may be combated. Any one of the many good preparations of iron may be used but, in general, it is well to avoid those having a marked stringent action such as are damaging to the teeth unless extreme precautions are taken, the organic preparations which in general seem to be far less efficient than the inorganic, and especially certain elaborate and superelegant pharmaceutical compounds of the shotgun variety which are best discarded entirely.

In certain instances of extremely obstinate chlorotic anemia it has been found a useful procedure to resort to repeated **small bleedings**, only from 4 to 6 ounces (113.4 to 170.10 grams) of blood being taken at a sitting. In a number of instances this has been shown to result in a renewed stimulation of the blood-forming tissues and an increased ability of the organism to bring about blood regeneration.

HYDROTHERAPY.—It is quite conceivable to the author that, as is so often stated, many instances of distinctive beneficial effects from **hydrotherapy** may be observed in its application to the treatment of chlorosis, and where it may be applied without undue fatigue to the patient and by one thoroughly conversant with its use, it is thoroughly proper and justifiable. In this as in so many other instances, however, one must be on his guard against the usual *post hoc propter hoc* method of reasoning which vitiates now as it always has done our whole therapeutic fabric. One should never forget that in the case of hydrotherapy it will seldom be found that other therapeutic measures are not being applied at the same time, and, furthermore, that simple anemias tend towards recovery when the causes are removed, under almost any treatment that is at all rational. A correct therapeusis merely reinforces the regenerative attempts of Nature herself and promotes a swifter and more permanent recovery. One need hardly say that any and every method which readily may be applied should be used.

Certain methods of hydrotherapy individually would be contra-indicated and these are especially such as would tax the strength and resistance of the patient in any way, for the cardinal principle, as heretofore stated, is the securing of rest. Sweating can hardly be a good method of procedure and indeed every sort of depressant should be avoided in these cases.

EXERCISE IN CHLOROSIS.—The great importance of absolute rest in certain of the more extreme types of chlorosis has been emphasized, and in those cases representing relapse or in which there is a decided or extreme chronicity, absolute rest over several weeks may be the prerequisite to the attainment of any good therapeutic results. As stated previously, all cases in which the anemia is pronounced should be treated in bed primarily if possible, as thereby the quickest and most satisfactory results are obtainable.

In this connection it must be borne in mind that in all anemias of high degree the cardiovascular system is involved and there is likely to be a peculiar circulatory instability and a greater or less degree of myocardial insufficiency.

It becomes important, therefore, oftentimes to treat these cases not only under rest but in such a way as will regulate carefully and systematically the resumption of physical activity. The patient who has been lying quietly in bed should not be permitted to get up and about freely in a few days, but should be inducted gradually into the old field of activities and at first protected carefully from exercise involving any real circulatory effort.

TREATMENT OF THE NERVOUS SYMPTOMS OF CHLOROSIS.—The management of a case of chlorosis from this viewpoint differs in no way from the general treatment of nervous conditions, and it is perfectly permissible to use sedatives such as the **brömids, veronal, sulphonal** and the like as indications arise. In the case of the excessively nervous individual under treatment in bed and in the hospital it is often of special importance and value to administer over considerable periods small doses of the bromids, or, better still, divided doses of veronal.

It is necessary at times to place these patients on a systematic long-continued rest cure, but, for the most part, cases of chlorosis, even though extremely severe and with very marked clinical symptoms, result in a prompt and satisfactory recovery.

Prognosis.—In cases of primary chlorosis, properly treated, the prognosis is good and recovery should take place in practically every instance. In actual practice, for reasons already stated, a considerable number of the primary cases do not result in complete recovery and some of these become and remain chronic. There can be no doubt that the persistence of blood impairment in any individual is an invitation to disease both acute and chronic, and constitutes a persisting impairment in the general health which may lead to breakdowns or be embraced in the term "chronic invalidism." A great number of women carry mild and even relatively severe grades of anemia all their lives.

Death does not result in any instance from chlorosis itself though it may occur by reason of a coëxisting gastric ulcer or the development of sinus and venous thromboses.

Pathology.—Inasmuch as chlorosis does not kill, little is known of its pathology and there are no changes which belong especially and peculiarly to this ailment.

IDIOPATHIC APLASTIC PERNICIOUS ANEMIA

Definition.—This term* is applied to a relatively uncommon pernicious form of anemia of unknown causation, nonhemolytic, showing, according to most recent statistics, male predominance (20 per cent.), falling chiefly between the ages of twenty and forty, but occurring in childhood and old age, in which the blood and autopsy findings show insufficiency and hypoplasia or, in typical cases, aplasia of erythropoietic tissue of the bone marrow. The disease is usually progressively and often rapidly fatal, resists transfusion, lacks the clinical signs of excessive hemolysis, is resistant to all therapeutic measures, and is distinctly more hemorrhagic in type than the ordinary form.

Etiology.—The cause of the disease is wholly unknown. It must be regarded and treated as a distinct type, for apparently selective and direct toxic bone-marrow destruction and aplastic insufficiency are the dominating features in its pathogenesis.

Insufficiency of the bone marrow may occur in the absence of aplasia and even when this substance is found at autopsy to be hyperplastic. It would appear that inhibition of the erythrogenetic function may arise from many causes, among which may be recurrent severe hemorrhages in the presence of a constant toxic factor. A mere arrest of erythrocyte proliferation will produce, of course, the blood-picture of defective hemogenesis.

---

* Many objections to this terminology have been urged of late, but none of them seem sufficiently weighty to justify its abandonment. This type of anemia *is* "aplastic" and "pernicious" and the use of the former term distinguishes it clearly from its opposite, "Addisonian anemia," also pernicious.

Quite logically aplasia of the bone marrow may attend the final stages of especially toxic cases of anemia primarily hemolytic such as that of trinitrotolual poisoning, Bothriocephalus anemia, or, in rare instances, the true Addisonian type. One must bear in mind also that aplastic anemia of known and specific causation may and does occur. This is best exemplified in certain instances of benzol poisoning and more rarely in profoundly toxic cases of diphtheria, sepsis, or even pneumonia. Over-roentgenization in the leukemias may produce partial or complete aplasia, but many cases of long-continued chronic anemia may show some aplastic areas in the bone marrow.

Symptomatology.—The disease is peculiarly insidious in development and far advanced usually before recourse is had to the physician. Progressive weakness preceded by fatigability is the invariable history. The patient is pale, sometimes strikingly so, but the yellowish tint of Addisonian pernicious anemia is wholly lacking, though several of the author's patients have shown a brownish tint or a gray pallor.

LABORATORY FINDINGS.—*Blood.*—The erythrocyte count is seldom much above 2,000,000, falls usually to a million or less, and one count as low as 110,000 is reported. The color index in rare instances may be low, but is usually normal or but slightly reduced, *i. e.* it corresponds pretty closely to the erythropenia.

In this disease, as in some instances of purpura hemorrhagica, the resistance of the red cells to salt solution is peculiar in that complete hemolysis occurs in a solution of higher strength than is required for the normal cell.

All forms of nucleated reds are absent or extremely scant. Poikilocytosis and anisocytosis are slight or wholly absent and polychromatophilia is not marked. Reticulated cells are usually markedly reduced in number or wholly absent but in some instances ephemeral increases occur. Leukopenia and relative lymphocytosis are present as in true pernicious anemia but in higher grade and the lymphocyte dominance is progressive. White cell counts under 200 are on record. The lymphocytosis is of the small type and results from the marked reduction of the polymorphonuclear cells and the absence of eosinophils.

The blood-platelet count is very low in most instances, reductions of 20 per cent. of the normal having been reported. Their size may be greater than normal and their deficiency in number is progressive as the disease advances. The *coagulation time* is lengthened and the hemorrhagic tendency often is pronounced. The *urine* is relatively light in color and free from an excess of urobilin and urobilinogen. The *liver, spleen* and *lymphatic glands* are not enlarged markedly if at all and, even though nucleated cells are present originally, they tend to disappear as the disease advances. Temporary splenic and hepatic tumefaction of moderate degree has been noted by the author in several cases.

Differential Diagnosis.—The picture is so directly opposite to that of Addisonian (plastic) pernicious anemia or the plastic secondary types of known toxic origin as to permit of no error in that direction. If aplasia occurs as an end stage of the foregoing, a number of abnormally large erythrocytes will be encountered in most instances and almost certainly the color index will remain high.

The pronounced blood-platelet shortage and high grade of leukopenia with relative lymphocytosis rules out high-grade secondary anemias of the usual type, and one of the most distinctive clinical features is the presence of a very low blood count with apparently normal erythrocytes. In temporary arrest of blood formation and indeed in nearly all conditions simulating the idiopathic aplastic pernicious anemia the blood count does not maintain the extreme low figures encountered in the idiopathic aplastic type; nevertheless, as stated, the diagnosis is always a tentative one unless confirmed by autopsy. The distinction between idiopathic anemia and idiopathic purpura hemorrhagica of the acute or subacute type may be impossible in certain instances.

Symptomatic purpura hemorrhagica occurs in many diseases amongst which is the one under discussion and the associated blood-picture in the idiopathic form varies from that of aplastic anemia, if at all, only in the presence of cells indicative of an attempt at blood regeneration. The platelet shortage occurs early in acute and subacute purpura hemorrhagica and the extreme anemia is much later in appearing than is the case in aplastic anemia.

Another puzzling condition is encountered in the nonleukemic phase of an acute lymphatic leukemia lacking the distinctive glandular changes. In such cases a distinction can be made usually because of the adherence of the lymphocytosis of aplastic anemia to the normal small cell type, whereas in acute lymphatic leukemia this is not true of its blood-picture. In the latter the leukocyte percentage is in most instances higher (90+ per cent.) than in aplastic pernicious anemia in which the lymphocytes seldom exceed 70 per cent. of the total.

Treatment.—So far no known treatment has proven of any great value in this form of progressive pernicious anemia and in all instances of the true idiopathic type the course is progressively, inexorably, and more or less rapidly fatal. The first and most imperative need is **absolute rest**; the second, **intelligent feeding.** No attempt need be made to lay down any set dietetic rules, for the cases must be individualized and in many instances the preferences of the patient outweigh any *a priori* assumptions as to his dietetic needs.

The failure to recognize the need of absolute rest, physical and mental, has proven the chief stumbling block to treatment in the past. The duration of absolute rest varies with individual cases, but must always represent a period of several weeks, and the **gradual** and **systematic resumption of activity and its after-limitation** is of equal importance.

The effect of overexertion may be and is often directly and promptly reflected in a lowered erythrocyte count; and in any profoundly anemic individual or even in cases of improvement, after a patient has been long inactive, very slight amounts of exercise may represent overexertion. Anything producing a subjective sense of *exhaustion* is distinctly harmful. Mere lassitude, a sense of persisting fatigue, may be and often is unescapable even though a high grade of improvement has been attained.

Months are required to produce results of any *permanence* even in favorable cases and the duration of the improvement is dependent largely upon the deliberate, systematic, gradual, and graduated increase of activity insisted upon by the physician. Finally, it should be said that in true idiopathic pernicious anemia, transfusion is futile and the disease is progressively and inexorably fatal.

Pathology.—Autopsy, which alone makes possible a positive diagnosis, reveals hypoplasia or complete aplasia of the bone marrow which is become mere fat, and in most instances multiple subserous punctate hemorrhages.

MYELOPHTHISIC ANEMIA

Definition.—This is a form of anemia due to the mechanical limitation of erythrogenetic tissue through invasion of the bone marrow by pathologic new growths plus abnormal stimulation of the invaded tissues. No extended description of this condition would be justified in this section, as the blood changes are merely a symptomatic result of any one of many conditions in which the invasion or mechanical destruction of bone-marrow tissue areas occur.

Osteosclerosis, chloroma, myeloma, lymphatic leukemia, and the metastases of carcinoma and hypernephroma furnish the commoner examples of this form of anemia. The blood-picture in this condition is variable, the most common findings being one characterized by the presence of large numbers of blasts and other immature cells referable to the bone marrow as their normal source. In some instances an excessive platelet decrease occurs and in others there may be such a decrease, but the blood-picture is not a constant one.

SIMPLE CHRONIC ANEMIA

(Associated with Defective Hematopoiesis)

Definition.—This is an anemia which is not definitely hemolytic, aplastic, or pernicious. It represents really a secondary, nonhemolytic type and presents no very characteristic picture.

Etiology.—To name the known conditions productive of such an anemia would exhaust nearly the entire list of known diseases. Acute and chronic infections, including focal infections, tuberculosis, and syphilis, exhausting chronic diseases, poor food, bad hygiene, an unfortunate environment, malignant disease, disorders of the ductless glands, and gastro-intestinal ailments, may be named as showing the breadth of association.

Any grade of anemia may exist but the great mass of such cases show relatively slight grades of hemoglobin deficit which usually runs parallel with the hemoglobin deficiency. Achromia is present but less marked than in chlorosis. Anisocytosis is seldom marked and nucleated reds ordinarily are absent. In some cases increased regenerative activity is present but this is not such as would lead one astray in diagnosis.

It is wholly probable that amongst these cases now and then, in certain instances, intervals of moderate grade hemolysis occur transiently, but the dominant feature is marrow insufficiency.

Treatment.—The treatment is essentially the same as that of chlorosis with somewhat more stress upon the administration of arsenic and the removal of the primary cause of the disease whenever possible.

ACUTE POSTHEMORRHAGIC ANEMIA

Definition.—This is an anemia due to the more or less sudden, rapid and extreme loss of blood or to rapidly repeated severe hemorrhages.

Symptomatology.—The symptoms of anemia due to actual loss of blood must vary widely with the amount of the hemorrhage and the condition of the individual at the time it occurs.

Furthermore the rate of flow must influence greatly the symptoms produced, introducing as it does the question of shock of greater or lesser severity. To a certain extent also the consciousness or unconsciousness of the patient at the time, and his own temperament enter into the symptoms produced by any considerable hemorrhage. A concealed hemorrhage of which a nervous high-strung patient is wholly unaware may produce less shock than an open one in which the blood loss is much less.

As a matter of practical importance one may add that the amount of blood lost in acute open hemorrhage is greatly overestimated by the patient and by those around him in most instances, and no symptoms of extreme blood loss may appear in the blood-picture even when the patient believes that a loss of ''quarts of blood'' has been sustained.

A robust adult has borne the loss of nearly or quite one-half his blood in certain instances, but the ability to withstand such drains is less at the younger ages and depends not only upon the previous state of health of the individual but also upon the rapidity of the flow and the circumstances surrounding the hemorrhage.

On the other hand enormous drains resulting from repeated small hemorrhages may be unattended by many of the group of symptoms associated commonly with large hemorrhages. Loss of total blood volume rapidly brought about is accountable for the symptoms of shock, subjective extreme exhaustion, actual collapse, faintness or actual syncope, sighing, rapid shallow breathing, restlessness, profuse sweating, and the like, so commonly observed in large acute hemorrhages. The suddenly induced oxygen shortage is,of course,a factor in certain of these.

The promptness with which such initial symptoms abate or subside following the cessation of bleeding, even though blood regeneration cannot have taken place, shows how great is this factor and how prompt is the adaptation of the tissues to the lesser volume under an emergency redistribution.

It must be remembered that even in considerable acute hemorrhages the factor of acute reduction in volume makes the blood count and hemoglobin estimation an uncertain guide, inasmuch as the amount of each in a given quantity of the blood may be affected but slightly. Some striking examples have come under the author's observation and in one especially an assumption of minor loss of blood might and would have been made if these factors alone had been considered in the face of the clinical fact that an almost fatal hemorrhage had occurred.

With improvement the blood-picture in such cases is of the chlorotic type, the hemoglobin deficit being greater than that of the blood-cells, *i. e.* the color index is low and for a time tends to drop because of the more rapid renewal of the erythrocytes in the process of blood regeneration. During this stage the stained smear will show abundant evidence of bone-marrow activity.

Blood-platelets rapidly increase in number, sometimes reaching a count of 1,000,000 per cubic millimeter; reticulated cells are plentiful;

nucleated reds appear; bone-marrow white cells (grandular leukocytes) may be present to a degree that raises the white count to double normal figures and there may be anisocytosis, polychromatophilia and even some degree of poikilocytosis. The white cell increase is of the polymorphonuclear type. The lymphocytes are unaffected.

Under such conditions the erythrocyte diameter is slightly less than normal. The platelets also are of less than normal diameter. On the other hand microcytes are usually absent. In recovery from severe acute hemorrhage it would appear that the replacement of water content, protein, and plasma is first completed, the red deficit is next adjusted and the hemoglobin shortage is the last factor to be wholly corrected.

CHRONIC POSTHEMORRHAGIC ANEMIA

Definition.—Anemias due to the repeated occurrence of open or concealed hemorrhages of greater or less amount, so frequently repeated as to prevent complete blood regeneration or exhaust the reparative powers of the blood-forming tissues are included here.

Etiology.—Among the many causes of this form of anemia are (*a*) bleeding hemorrhoids; (*b*) gastric and duodenal ulcer; (*c*) menorrhagia from whatever cause; (*d*) helminthiasis (hookworm, etc.); (*e*) carcinoma of the bowel; (*f*) recurrent severe epistaxis; (*g*) hepatic cirrhosis; (*h*) hemophilia; (*i*) scorbutus; (*j*) severe purpuras; and (*k*) repeated hemoptysis.

Symptomatology.—The general symptoms are such as have been described under the anemias and vary in degree with the severity of the anemia and the general condition of the patient. The grade of anemia in this type may be very slight or extremely severe. The blood-picture varies accordingly and is not of itself characteristic.

In cases of ordinary severity seen a considerable time after any hemorrhage has occurred, the deficit in erythrocytes and hemoglobin runs nearly parallel though achromia may be present. With any renewal of hemorrhage the signs of active regeneration appear unless the marrow has lost its responsiveness to such a stimulus. Blood-platelets are increased following any hemorrhage unless the marrow has become insufficient.

Diagnosis.—It will be noted that the diagnosis depends in most instances upon the anamnesis. In its very severe form it produces a picture superficially resembling Addisonian anemia. All of the characteristics of hemolysis are lacking, however, and the misleading factors are only such as indicate blood regeneration.

The color index is not high save in the rarest instances, but low or parallel with the erythrocyte percentage. Of the nucleated red cells present the normoblast predominates and the average size of the non-nucleated forms is normal or low. Very marked differences in size seldom appear and the large oval reds so often present in pernicious anemia are either absent wholly or few in number. The urine and stools show no pathologic amounts of urobilin.

Treatment and Prognosis.—The treatment and prognosis alike depend largely upon the removal of the cause; the therapeutic indications otherwise are those of chlorosis, with emphasis upon the value of **arsenic** either alone or in combination with some form of **iron.**

ADDISONIAN PERNICIOUS ANEMIA

(*Hemolytic Pernicious Anemia*)

Definition.—This is a primary anemia, probably invariably fatal, progressing slowly by remission and relapse, characterized by hemolysis and perverted hemogenesis associated with progressive and ultimately fatal extreme diminution in the number of erythrocytes in the circulating blood, the appearance of large numbers of immature red blood-cells, and a marked reduction in the hemoglobin with a relatively high individual cell hemoglobin content which results in a high color index.

Etiology.—Despite the many attempts to place this disease on an actual etiologic foundation nothing definite is known at the present time with relation to its causation.

AGE.—The disease occurs usually in middle age, is excessively rare in childhood and in very old persons, and most frequently encountered between the fortieth and fiftieth years.

SEX.—In the United States and in England males are attacked more frequently; in Germany female cases seem to predominate.

MANIFESTATIONS.—In the Addisonian form of pernicious anemia the dominant and invariable characteristic is an excessive, relatively intractable, slowly progressive, and ultimately fatal hemolysis. A condition exactly similar has followed Bothriocephalus infection and pyridin poisoning in which one deals with known hemolysins, and it would seem that certain unknown toxins acting in small but potent doses over long periods stimulate abnormally the hemolytic activity of the bone marrow, spleen, and lymph glands. As a result of such continued overstimulation and persistent hemolysis the erythrogenetic centers themselves become overactive and cause that ultimate dominance of the large immature vulnerable erythrocyte and erythroblast which dominate the blood-picture of this disease.

Special stress has been laid by Grawitz upon the well-known shortage or entire absence of free HCl in the stomach contents of these cases. He believes that this results in excessive albuminous putrefaction and a weakening of the defensive mechanism against bacterial activity.

It would seem possible that the ultimate cause may be found in the selective activity of peculiarly virulent hemolytic streptococci, yet the elimination of hidden septic foci has not produced a striking result even with relation to amelioration, much less cure, of this disease.

OTHER HEMOLYTIC ANEMIAS.—It must be remembered that certain variants which were included erroneously by Leube and Arneth under the term "leukemia" should really be entitled to no separate classification.

Quite aside from these one may also encounter anemias of the hemolytic type associated with carcinoma of the stomach with ulceration and concurrent hepatic metastases. So also in pregnancy, the puerperium, and in syphilis, one finds cases of anemia distinctly of the hemolytic type and presenting a clinical picture almost or wholly identical with that of the true Addisonian type. No separate formal classification should be attempted, as the chief difference is one of curability on the one hand and the presence, in the case of the gastric carcinoma with metastases, of a purely secondary anemia, which has taken on the hemolytic form.

Anemia pseudoleukemia infantum is not a clinical entity and deserves no separate classification, inasmuch as it embraces usually nearly every symptom of Addisonian pernicious anemia plus splenomegaly. Such variants as are represented by an unusual polymorphonuclear increase, or the occurrence of myelocytes are probably related to the age of the patient and are of no special importance.

Symptomatology.—CLINICAL HISTORY.—The disease is peculiarly insidious in onset and in public clinics and private practice alike the great majority of the cases encountered show a primary erythrocyte count under 2,000,000. It is a rare exception and usually a purely fortuitous circumstance when one encounters a genuinely early case.

Impairment of strength is usually a prominent feature varying, however, all the way from slightly increased fatigability to extreme exhaustion. Such symptoms may date back for many months or for several years in their milder degrees, but seldom have been sufficient to attract serious attention save during the few months preceding the oncoming of more serious symptoms.

Outward Appearance of Patient.—To an astonishing degree the victims of confirmed Addisonian pernicious anemia present an extremely suggestive and sometimes quite classical physiognomy. The superficial fat is well preserved until very late in the disease as a rule, and the skin, peculiarly smooth and velvety, carries the delicate lemon-yellow tint which is so prominent an outward sign of the fully-developed disease.

This peculiar color is obviously due to an hemolytic jaundice inseparable from so excessive a blood destruction as is present in these cases and is not absolutely distinctive of the particular disease under discussion. It is by no means always present and must be regarded as a relatively late symptom or at least one slowly produced by excessive hemolysis and indicative of a saturation of the skin with blood pigment. Nevertheless it is present to some degree usually by the time the patient is driven to consult a physician. It waxes and wanes both in skin and conjunctivæ with the varying phases of hemolysis and in association with the preservation of the subcutaneous fat constitutes a striking and valuable physiognomonic sign of the disease.

If seen first as an ambulant patient, as is usually the case, evidence of decided or even extreme weakness may be apparent and an exertion dyspnea may be obvious. It is always difficult to get any definite point of departure so far as the time element is concerned, so gradually does the disease progress and so insidiously does it overwhelm its possessor.

The first examination, apart from the blood-picture to be described later, shows little that is peculiar or characteristic. The muscles, as the disease advances, oftentimes are jellylike in their flabbiness to a degree found in no other chronic progressive or acute disease known to the author. Actual severe weight loss is absent in about two-thirds of the cases up to the terminal stages of the disease.

A matter of interest and of some importance is the fact that in the remissions any existing weight loss may be wholly or in large part regained —a fact of some significance in the differential diagnosis inasmuch as cases of carcinoma with like blood changes do not exhibit this power to regain lost weight.

HEART AND BLOOD-VESSELS.—All fatal cases of pernicious anemia are associated with a fatty degeneration of the heart which may reach the most extreme type and in many instances this results in a considerable enlargement of the heart and marked atonicity and loss of contractility which, together with the diminished hemoglobin and total blood volume, account for the extreme prostration so often encountered in these cases.

Many patients suffer great distress from recurring "palpitation." Faintness, oddly enough, is not troublesome as a rule until very late in the disease when syncopal attacks may occur under almost any grade of exertion on the part of the patient and make difficult the fresh-air living which ought to be his portion if possible.

Anemic Bruits.—In pernicious anemia, as in extreme degrees of anemia from whatever cause, the actual rapidity of the blood stream is greatly increased, the heart muscle is badly nourished, tends to become atonic and the same condition is doubtless reflected in the great vessels of the heart. Furthermore, the specific gravity of the blood is lowered decidedly. Thus we find present just the conditions which might produce bruits and these are invariably present. They are soft in quality usually, though occasionally harsh, almost invariably systolic in time and maximal in the great majority of the cases at the second left (pulmonary) interspace.

Systolic bruits may also be heard over the aortic area, second right interspace and at the apex, and in a very few instances, one of which has been reported by the author, a diastolic aortic murmur has been present during life, obviously due to dilatation of the aortic ring as no changes were demonstrable at autopsy. Vertigo is a troublesome symptom occasionally, as is also tinnitus aurium.

Gastro-intestinal Tract.—A recurrent "sore mouth" and tongue not infrequently attend the development of a case of Addisonian anemia and find a place in the anamnesis. This may have assumed the form of a mere hyperesthesia or may have been a definite stomatitis, simple or ulcerative. Needless to say such symptoms are neither constant in nor peculiar to this disease as has been asserted by some writers.

Ordinarily there is nothing of importance in the way of physical signs in the gastro-intestinal tract although in certain instances the severest symptoms may arise and contribute largely to the shortening of the life of the patient. These in most instances are distinctly periodic in occurrence. Almost invariably there is impaired appetite which varies from mere capriciousness to actual repugnance for food. Indeed this may prove one of the most troublesome features with respect to the treatment in a case of this disease. In certain instances this anorexia may be most pronounced in the earlier stages and become less prominent as the patient draws near the end after having experienced one or more remissions of varying duration.

On the other hand there may be most violent recurrent attacks of diarrhea and sometimes most troublesome intervals of food intolerance and actual vomiting. Needless to say the occurrence of such complications rapidly exhausts the already weakened patient. Constipation, persistent or alternating with diarrhea, is not uncommon.

Pain in the epigastrium, or more commonly a sense of discomfort, is encountered not infrequently and may prove a troublesome symptom. Flatulence is another factor to be dealt with and sometimes constitutes a source of great annoyance to the patient. Epigastric distress is observed in many cases; actual severe pain of a paroxysmal type occurs less frequently, and should suggest always an especially careful investigation of the condition of the spinal cord. The liver is seldom much enlarged but may be easily palpable in cases of long duration.

The spleen varies greatly in size but is always of denser consistency than normal. Any decided enlargement usually occurs quite late in the course of the ailment and one seldom finds a border more than one inch below the costal margin. It is palpable in about 50 per cent. of the established cases.

The Stomach Contents.—In all established cases of Addisonian pernicious anemia the gastric secretions are impaired and in the larger number (90+ per cent.) there is an actual absence of free HCl. It is altogether probable, moreover, that it is a relatively early manifestation and may account for the remote history of "indigestion" or "dyspepsia" so often a part of the anamnesis.

The Stools.—The character of the stools is variable, but wherever there are direct gastro-intestinal disturbances and an especially active hemolysis one is likely to find that the stool carries a peculiar chrome (brownish-yellow) color. In certain instances the bowel disturbance may be so great as to lead to an erroneous diagnosis of ulceration of the bowel, or the mucus content may be so high as to lead one to the erroneous diagnosis of a mucous colitis. A positive blood reaction is not at all uncommon.

Genito-urinary System.—In both the urine and in the stool one finds an indication of the hemolytic activity in the presence of urobilin. The specific gravity of the urine is usually low and the color brown, this being intensified in relapses. A transient or cyclical albuminuria may occur during the earlier stages of the disease and occasionally one encounters a case which seems to be associated definitely with an established chronic nephritis. The kidney function is often disturbed either persistently or periodically; acidosis may occur, and in these individuals an uremia may be at least a contributory cause of death.

Nervous and Mental Symptoms.—As a rule the patient with a fully developed pernicious anemia is philosophic and calm, but occasionally one finds the excessive irritability so generally encountered in connection with other severe anemias. In certain individuals the inability to sleep or to secure restful slumber is a source of very great inconvenience and contributes to the progressive weakness.

It is stated by Gulland and Goodall and other observers that mental symptoms were very prominent in a small proportion of their cases and reference is made to maniacal attacks, hallucinations and delirium occurring as terminal manifestations. Indeed it would appear that almost any form of mental disturbance may occur in association with or as a part of Addisonian anemia.

The author's experience has been extremely limited with respect to this complication but there can be no doubt that such symptoms occur early in certain rare instances and more commonly in advanced and intractable cases and are associated with demonstrable areas of degeneration in the brain. These are similar to those found in the spinal cord in this disease.

A subacute combined sclerosis of the cord is a common feature resulting in patchy degeneration and this no doubt accounts for the tingling and numbness in the feet and legs, less often in the upper extremities, which is a matter of complaint in about one-third of the cases of Addisonian pernicious anemia. In a far greater proportion of cases involvement of the central nervous system is demonstrable under careful investigation. Indeed in patients above fifty years of age it is probable that between 80 and 85 per cent. carry such cord changes. The frequency of their occurrence is not dependent upon the grade of hemolysis present in the given case and decided symptoms referable to the spinal cord may precede any striking changes in the blood.

In some instances the deep reflexes are diminished or lost and there may be a sexual erethism. Indeed the symptoms of degeneration of the spinal cord itself may take either the form of a tabes or a lateral sclerosis, but oftener there seems to be a combination of anterior and posterior column disturbance. Furthermore, the irregularity of lesion distribution or the presence of cord hemorrhages may give rise to suggestively bizarre manifestations. Myelitis rarely occurs but multiple neuritis is occasionally encountered. The development of symptoms and signs referable to the central nervous system is usually very gradual.

Special Senses.—Dimness of vision, retinal flashes, conjunctival hemorrhages and edema of the eyelids, especially of the lower, are symptoms not infrequently encountered. The optic disc is pale and not infrequently one finds retinal hemorrhages. Progressive deafness is occasionally observed and in one or two instances the author has noted great impairment or even perversion of taste and smell.

Body Temperature.—For months or years the temperature may be quite normal or there may be an intermittent temperature, usually not extreme, from the time that the patient is first seen by the physician. As a rule it does not run high even in the terminal stages of the disease, usually reaching about 102° F. (38.89° C.) at night. It demands no treatment of any kind but directly contributes to the weakening of the patient.

The Skin.—The peculiar lemon-yellow tint of the skin so frequently seen in this disease has been referred to in a preceding paragraph. It should be stated emphatically that this tint is not invariably present, so that one must not be deceived by its absence into overlooking so serious a disease as Addisonian pernicious anemia.

The Blood-picture.—As it flows after puncture, the blood of advanced cases appears, usually, pale and thin and actually seems to *slip* from the skin. Dropped on a piece of white filter paper, an outer zone of faint gray surrounds the central red. In marked remissions or cases but slightly advanced both these characteristics may be lacking.

The total blood volume is lessened in these cases, the color index is high, the specific gravity of the blood is diminished, blood-platelets and fibrin alike are diminished markedly and the "coagulation time" is increased, so that bleeding from the ear may continue languidly for some time but is not likely to prove excessive.

As stated previously, it is the rule rather than the exception to find the red blood count under 2,000,000 at the first examination. The lowest initial blood count observed by the author was 348,000 erythrocytes per cubic millimeter.

The hemoglobin is reduced greatly and may be below 15 per cent. in cases of extreme hemolysis. The errors attending the estimation of hemoglobin by the clinical methods in use are accentuated when the percentage reaches low figures and oftentimes a better idea of the hemoglobin content is gained by the microscopical appearance of the erythrocytes.

Poikilocytosis (cell deformity) is marked in all severe cases and the "anvil" and "pear-shaped" forms are very plentiful. Practically every known abnormal variation in the red cell is found in the blood-picture of Addisonian anemia when the hemolysis is active.

The red cells vary greatly in size (anisocytosis); macrocytes and microcytes are numerous, and giant nucleated and nonnucleated red cells are present invariably and in large numbers in the so-called blood crises, though otherwise they are found only after careful search and in small numbers. The average diameter of the red cell is usually increased and this constitutes a clinical point of importance in diagnosis.

Polychromatophilia, that is, irregularity in staining, is a marked characteristic in this disease though by no means peculiar to it. The large, deeply stained oval or otherwise deformed cell is peculiarly striking and somewhat distinctive and the finding of such cells in any blood should arouse suspicion.

In three-fourths of all cases the total number of leukocytes is below normal and this leukopenia may be extreme, the average being less than one-half the normal count. In some instances there is an absolute reduction of the polymorphonuclears leading to a relative lymphocytosis. Myelocytes and the erythrocytes showing basophil granules with Wright's stain are present nearly always but in small numbers. In this form of pernicious anemia when the blood-picture is pronounced and nucleated reds are present, the megaloblasts should outnumber the normoblasts or a diagnosis should be held in abeyance until this can be established.

Blast crises, during which an immense number of nucleated red cells appear, are relatively common in Addisonian pernicious anemia and their occurrence is a bad portent. They seem to represent overstimulation of the diseased marrow such as would be followed logically by a reaction of increased insufficiency and further marrow destruction. In severe secondary anemias of the hemolytic type a relative excess of normoblasts or microblasts usually exists.

It should be remembered that during remissions with an erythrocyte count of 3,000,000 or more the blood-picture may appear almost wholly normal. Almost invariably some concrete evidence of the basic disease may be discovered in the stained smear.

Diagnosis.—Obviously the diagnosis of pernicious anemia must be made from an examination of the stained blood smear and from this only can a positive decision be reached. In many instances nevertheless a diagnosis may be made at sight from the physiognomy and general appearance of the patient alone with a reasonable degree of accuracy. The high color index, a leukopenia, the presence and especially the predominance of megaloblasts with respect to the nucleated erythrocytes is the keystone of the diagnostic arch.

If the blood findings are confusing at the time the patient is first seen, there will nevertheless be a definite severe anemia and a greater or less degree of physical weakness which is most suggestive; and, furthermore, very early in this disease a high color index is likely to be present and is suggestive even in the absence of the typical blood changes and physiognomy. The presence of fever is sometimes very misleading and it is not uncommon to encounter cases in which tuberculosis or sepsis has been the diagnosis.

Complications.—It is difficult to deal with the complications of pernicious anemia formally, for to the author these seem to be not so much complications as accompaniments and mere coincidences. Fever, relatively intractible vomiting and diarrhea, spinal cord changes, extreme cardiac weakness and uremic manifestations from decided kidney involvement are the chief complications encountered in this disease. There are no sequelæ in pernicious anemia and it does its own killing most effectively.

The one case of apparent complete recovery known to the author occurred in his own practice during the past decade, the patient having lived ten years after making a complete recovery and coming into the hospital only to die of another ailment.

Association with Other Diseases.—There are no definite disease associations in the case of the Addisonian pernicious anemia so far as has been ascertained, but the disease has been associated in the past with a great number of conditions to each of which a more or less important place was given in the etiology of the disease. Syphilis, malaria and nephritis are the three conditions most frequently so associated.

Clinical Varieties and Types.—As has been stated previously, pernicious anemia permits a considerable number of variants and it is doubtless a mistake to accept as individual diseases or even syndromes the large number of cases reported from the continent, inasmuch as these represent usually merely a small group of especially variant cases.

With respect to the course of the disease, it is possible to distinguish several distinct types. In elderly people especially there is a tendency to slower progression on the part of the disease process with remissions only slightly or but moderately defined in some instances and steady, slow continuous progression in others. At the other extreme, one may encounter cases which are of relatively short duration, almost acute in type, and wholly without remission. Between these lie the cases of the type encountered usually which are characterized by remission and relapse of marked degree. In one instance the author has seen a ten-year interval of complete immunity and a wholly normal blood-picture. In others long periods varying from several months to several years occur. In yet others the remissions are shorter and the blood improvement less marked.

Treatment.—PRELIMINARY COMMENT.—Primarily it must be remembered that Addisonian pernicious anemia, so far as known, is a fatal disease and all that can be done is to retard its progress and remove or ameliorate so far as is possible its various symptoms as these arise.

One group of symptoms of this disease is quite beyond treatment, namely, those due to involvement of the cerebrospinal system. On the other hand, in the great majority of instances, practically every other symptom which may arise may be relieved, for these cases, even when of an established and advanced type, tend to make temporary improvement, slight or marked, or even an apparent recovery extending over several or many years. In other words, the disease is one which in its usual form progresses very gradually by remissions and relapses of varying duration which may be repeated many times.

There can be no doubt that in certain rare instances the duration of such a case may be as long as two decades but the longest interval of improvement personally encountered by the author and previously reported in St. Paul, Minn., was ten years. In this case, however, there was apparent complete recovery from the Addisonian anemia and the patient died of a disease wholly unrelated to the former.

No patient of this type is too ill to afford some slight hope of obtaining a remission, provided the attack is the first one which the patient has suffered. With each succeeding relapse the difficulty of securing a marked improvement is increased and the duration of the remission tends to grow shorter with recurring relapses, if these occur. The author has treated cases through as many as six and seven of these exacerbations and there are on record instances where fifteen or even more remissions and relapses have occurred.

REST.—Unquestionably the most important and fundamental therapeutic measure in the treatment of this ailment is **rest, physical and mental**, and indeed this statement applies to all forms of severe anemia whether acute, subacute or chronic. In the case of Addisonian pernicious anemia particularly, physical rest especially meets the cardinal therapeutic indications, for in no other disease do we see so generally a patient presenting himself to the physician for the first time with a fatal ailment in an established and advanced stage.

In the great majority of instances serious changes have already occurred not alone in the bone marrow but also in the heart of the individual. In some instances extreme weakness is manifest and in nearly all fatigability and a lessened field of response to effort, especially on the physical side, are symptoms either obvious or readily elicited. Nearly all such cases therefore have been active for a considerable period under conditions which have represented a more or less severe physical overstrain which could not fail to accelerate and intensify the morbid process.

Exceptions to the rule as stated above, of course, do occur, and in rare instances, and usually quite fortuitously, the diagnosis of Addisonian pernicious anemia is made at what may be a relatively early stage when there are no marked signs of hemolysis and constitutional symptoms are slight or even wholly absent. Even in such cases, however, the physician who is wise will secure for the patient as much physical relaxation as is feasible without putting him absolutely in bed and will watch the effect of physical and mental effort upon the blood-picture and keep the patient under reasonably close observation.

Whenever possible, **absolute rest in bed** is enforced and the patient should be in a **hospital** and, when his circumstances permit, under the direct care of a **special nurse**. Every effort should be made to combine with this complete relief from physical effort, the greatest possible degree of mental rest and relaxation. This latter point is one of great importance yet oftentimes overlooked or dealt with in a more or less slipshod manner. Obviously the number of visitors should be reduced to the minimum and these should be most carefully selected. In many cases it is better for a time to permit **no visitors** or only some one member of the family, and in all cases an effort should be made to relieve the patient from over-volubility, excessive interrogation, and the type of gossip who loves to carry about depressing information.

The duration of absolute rest in bed never can be made a fixed term but must be varied according to the initial condition of the patient and also with the degree of his improvement as measured by the general physical condition and especially by the blood-picture. Whenever circumstances will permit, gentle but thorough **massage** and slightly resisted movements should be undertaken from the start. This is especially necessary in the anemias of this type because of the readiness with which the muscles become flaccid and the physical strength impaired.

The resumption of physical activity should be preceded invariably by periods when the patient may be sitting out of bed, preferably in the open air, these being lengthened a few minutes each day and no attempt at active progression permitted until the patient can sit up without fatigue for an hour or two at a time twice a day. When this period is reached he may be permitted to take a certain number of steps with support, these being increased each day according to the effect produced upon the patient with relation to fatigue care being taken always to permit no effort which actually tires him. The author does not consider it wise to attempt exercise other than walking and personally does not use any form of gymnastics in such cases.

When the circumstances are favorable, after a period varying from six weeks to several months, the patient will be able to walk considerable distances without fatigue and should have been permitted gradually to ascend steps so that upon his return home he can do a reasonable amount of stair-climbing without exhaustion or severe fatigue.

Especial care should be taken to guard the patient against undertaking exercise to which he is unaccustomed. He must be inducted gradually into every new phase of physical effort inasmuch as the use of unaccustomed neuromuscular units is often attended by a degree of exhaustion many fold greater than that resulting from a far greater physical output along lines to which the patient has become habituated.

In connection with severe anemias no less than in the treatment of myocardial insufficiency of the primary type, the author knows of no error so common and so disastrous as is the failure to follow that sovereign remedy, physical rest, by intelligently regulated and specifically prescribed exercise.

Many patients, and especially those seen in public outpatient services, cannot be given the benefit of the somewhat elaborate regimen outlined in the foregoing paragraphs and in some instances it is absolutely necessary for the unfortunate victim of Addisonian anemia to continue to carry on household duties or attend to the duties necessary to a livelihood as long as he can stand upon his feet. Even in such cases, however, it is possible to secure periods of absolute rest, and in addition a very considerable expenditure of strength can be prevented by having such a patient perform every duty which can be so undertaken in a recumbent or sitting posture. During the twenty-four hours of the day a very great physical output occurs which is wholly unnecessary and due simply to habit and the lack of any necessity for attention to the securing of a maximum degree of physical rest.

According to the author's experience patients with pernicious anemia coming to the public clinic are usually in such a state as to make admission to a public hospital imperative, having very thoroughly exhausted their capacity for any sort of sustained effort prior to their visit to the clinic. After admission to the hospital such cases oftentimes show a degree of improvement and tendency to remission which is even greater than that found in cases of a similar confirmed and advanced type encountered in private practice.

FOOD AND FEEDING.—One of the commonest symptoms of pernicious anemia of the Addisonian type is anorexia, and this lack of appetite in some instances is associated with a positive food repulsion. Underlying these symptoms in a large majority of such cases there is an achylia gastrica and a decided tendency, as the disease advances, to gastro-intestinal upsets more commonly assuming the form of diarrhea and troublesome flatulence but occasionally associated also with decided nausea and at times vomiting.

These attacks do not differ in any material way from the similar seizures encountered in connection with achylia gastrica existing in the absence of pernicious anemia when that disease is of long standing and the demand upon the duodenal secretion has for the time being exceeded the power of the secreting glands. Obviously the indication in such cases is for a strict temporary limitation of feeding which must vary with the individual case and be determined largely by the degree of disturbance on the one hand and the nutritional state of the patient on the other.

Antifermentative remedies are of some use in such cases and the attacks of diarrhea may be treated symptomatically. These are sometimes very persistent and in some instances flushing of the lower bowel seems productive of much relief. A great deal may be done to reduce the severity and frequency of such attacks and diminish or prevent any excessive flatulence through the proper feeding of the patient. One of the commonest errors known to the author in connection with the care of the patient in bed is the tendency to use liquid diet. The ill-effects of a **milk diet** in many individuals are fairly well understood but stress should be laid upon the importance of using a minimum amount of liquid for feeding purposes, however,much water may be allowed between meals.

It is far better to administer milk, broths and soups with crackers or bread, cooked rice, or what not incorporated with them so as to make the diet so far as possible not liquid but semisolid. In some instances it is better still to cut out even the semisolid diet and substitute **light dry feedings.** In this same connection it is important to remember that the avoidance of fruit and fruit juices will often make the difference between comfort and discomfort or the avoidance or invitation of serious bowel attacks in bedridden patients. This would seem to be especially true of fruit taken during the afternoon or evening; and of those types of fruits which are artificially ripened, the chief offender, according to the author's observation of the citrous fruits, is the grapefruit: and in several instances cases have been observed in which an actual spastic constipation resulted from the excessive use of this article of food.

The author would not be understood as meaning that all fruit juices and the fruit itself cannot be used in the greater number of cases without harm, but would simply stress the fact that, where there is any tendency to flatulence or to attacks of diarrhea, attention to the foregoing rules will prove of definite value in treatment.

With respect to nutrition one encounters in Addisonian pernicious anemia two somewhat distinct types. In one, nutrition seems to be fairly well preserved for a long time; in others, it is markedly impaired. Cases of the former type should not be confused with those which carry a wholly spurious appearance of good nutrition, inasmuch as in some of the most advanced cases not far removed from the funeral period one may see a well-preserved panniculus adiposus and yet find underlying that muscles which feel like jelly and a degree of weakness wholly out of accord with the outward appearance of the patient. Indeed it seldom happens that patients with pernicious anemia as encountered in practice can safely be placed upon any diet save that which represents full nutrition or hypernutrition.

Nor is it wise in these cases to attempt to prescribe arbitrarily a set diet. The capricious appetite and the anorexia so often encountered make it necessary to leave the choice of foods, so far as may be possible, to any existing inclination on the part of the patient and, if this be lacking, to make the diet as varied and attractive as possible.

Ordinarily no one class of food need be omitted and, when the circumstances of the individual permit the degree of care represented by the trained nurse, or when, in the absence of hospital residence, he is ill at a home which can afford him some of the luxuries of the table, he should have these and they should be served in the most attractive manner possible.

It is held generally that the **red meats** and a **proteid diet** are peculiarly valuable to such patients, and this doubtless is true, but the **carbohydrates** and the **hydrocarbons** alike have an important place usually in the maintenance of his nutrition. The same may be said specifically of **eggs** and of the **green vegetables.**

Finally, it should be stated that there should be the most careful avoidance of any attempt at giving too infrequent feedings and too heavy a meal at any one time. The patient should have six feedings a day whenever possible and something once or twice during the night if he is awake.

FRESH AIR.—In no class of cases is **fresh air** more important to the patient and it is often wise to violate the rule of absolute rest in bed for the sake of getting the patient into a wheel chair, and out into the air and sunshine. If this is impossible owing to the peculiarities of his environment, he should be in a room which receives the maximum amount of sun and should spend the greater part of the day with windows open.

On the other hand it must be remembered that patients of this type are peculiarly susceptible to cold, often suffering genuine discomfort from the subjective sensation of chilliness. They should be protected, therefore, from chilling and the most careful attention paid to protection from cold. If proper precautions are taken with regard to this matter even very sick patients may with benefit be outdoors and in the sunshine even in winter weather.

DRUGS.—Iron has proven almost wholly valueless in Addisonian anemia though it has some more or less problematic value in cases which have attained a reasonably high blood count and approximately normal picture during a period of improvement.

Arsenic,on the other hand,the author believes to have a certain definite value in a considerable proportion of these cases. The fact that it does not in all probability ordinarily retard hemolysis or stimulate or regulate in any way blood formation is quite beside the point. The important fact is that a very great many patients improve decidedly under the administration of arsenic at periods when their progress is apparently arrested.

In the author's personal experience it has seemed to him that the highest degrees of improvement and the most favorable action of this drug are obtained by its use in moderate or even small doses over relatively long periods and in the careful avoidance of any of its toxic effects. He believes it to be a mistake to push the drug until even edema of the eyelids becomes manifest or to attempt to push its administration to a point where gastric discomfort becomes manifest.

Fowler's solution is the form in which the drug is most used even at the present time and this may be employed for long periods in small doses with advantage and without producing serious symptoms save where any idiosyncrasy exists. It is not necessary to administer it continuously; far better, the author believes, interruptedly, permitting periods of a week to elapse and commencing again with small doses of two or three drops and running these up to ten or twelve, always with high dilution. If it be thought undesirable to use the drug by the stomach, the **sodium**

cacodylate may be used hypodermatically and intramuscularly in doses of from 0.03 to 0.06 gram ($\frac{1}{2}$ to 1.003 grains).

Salvarsan has a certain number of able advocates and if used should be administered in small doses. The author's experience with **bone marrow** freshly prepared according to the formula of Professor Fraser has been such as to encourage him to continue its use as one of the therapeutic substances affording some aid at least in this disease.

TRANSFUSION.—There is so much of the dramatic element in the **transfusion of the blood** of a living person into the veins of another, and the procedure is so popular with the public press and the laity at large as to lead to a world-wide overestimation of its beneficial possibilities. It is to be hoped that the better evaluation of heroism resulting from the World War will make the public understand that a procedure which involves risk only to the recipient of the blood and none whatever to the person offering it is a rather commonplace affair.

It would be fortunate if a better estimate of this mode of treatment on the part of the laity might be obtained. The expectation that it will be used in all severe cases of anemia and the exaggerated idea of its effectiveness which prevails lead to a great deal of pressure upon the attending physician and in a great many instances to the employment of a measure which has but a limited use and may be potent for harm. It is to be hoped also that a critical study of the results of this procedure on the part of the practicing physician will lead to a better conception of the relatively limited field in which it proves a valuable agent.

The Field of Transfusion.—In Addisionian anemia the procedure neither cures the patient nor materially prolongs his life. The author's observation would indicate that it is incapable of initiating any remission which might not be expected reasonably to occur in the absence of the procedure. On the other hand he feels that such remissions as follow transfusion are shorter than those which occur spontaneously or under the ordinary treatment and that on the whole the procedure shortens materially the life of the patient.

That transfusion, properly performed, gives temporary relief in some instances cannot be doubted, nor can it be denied that serious and fatal reactions occur from errors in technic or from failure to understand the exacting nature of this procedure.

Transfusion does not inhibit or even retard hemolysis. It does mechanically increase the number of blood-cells, raise temporarily the blood volume, probably stimulates the bone marrow to increased activity as indicated by a heightened platelet count and an increased percentage in the white cells of marrow origin, and presumably may cause a temporary redistribution of all of the cellular elements of the blood. In some instances the young erythrocytes themselves show an increase; in others none occurs.

On the other hand these changes in the blood composition are temporary and relatively evanescent. The persisting level of cellular content is raised but slightly and it may be that the abrupt primary stimulation of a diseased bone marrow is neither a wise nor a rational therapeutic procedure. Certainly it is one to be employed only with a thorough and clinical understanding of the conditions under which it may do good and the many possibilities which it possesses for harmful action.

The more striking effects of transfusion as shown in the blood-picture make their appearance within twenty-four hours. In certain instances the reaction to marrow stimulation is extreme and unquestionably such cases at least suffer harm from the procedure. The persistence of the transfused platelet in the blood of the patient is of only a few days' duration; that of the white cells somewhat longer. The life of the transfused erythrocytes depends largely upon the severity of the hemolytic process but may endure probably for thirty days or even longer in favorable cases.

The results of successful transfusion as indicated by such changes in the blood-picture must be reflected in the temporary relief or amelioration of any preëxisting active symptoms such as (*a*) fever; (*b*) excessive rapidity and lability of the pulse; (*c*) dyspnea or precordial oppression; (*d*) excessively low blood-pressure; (*e*) anorexia; (*f*) subjective weakness, sense of prostration, recurring faintness, vertigo, etc.; (*g*) gastro-intestinal disturbances; and (*h*) excessive metabolism (10+).

The oft-repeated statements of the past that transfusion not only brings about amelioration of existing symptoms but permanent remissions is not sustained with respect to the latter by present-day statistics, nor does it conform to the somewhat extended experience of the author with this disease.

It is doubtless a justifiable procedure when distressing and exhausting symptoms of an urgent nature resist other therapeutic measures, but a hasty resort to it and its frequent repetition shows a regrettable tendency of the times, representing as stated previously, a faulty conception on the part of the laity.

That the remissions following successful transfusion are of shorter duration than those occurring apart from its use, the author believes firmly. It is a significant fact that the best results claimed for transfusion in Addisonian anemia are referred to those types of the disease in which spontaneous remissions occur.

If the transfusion is to be done, however, it should be timely and not be delayed until the patient is essentially moribund as is so often the case. Under no circumstances should it be attempted during an active hemolytic crisis. On the other hand it may be accomplished successfully even in very sick patients.

Prognosis.—It is futile to attempt to place a time limit upon the duration of a case of Addisonian anemia. One cannot state even the average duration of cases observed and reported. The beginnings of the disease are obscured by the absence of any striking general symptoms which would direct attention to the blood-picture and in consequence our knowledge is limited to the after-duration of cases seen first when the disease is fully established or, too often, when far advanced in its terminal phase. Save in the case of those last mentioned, death seldom occurs under six months, even in the more rapidly progressive type.

Commonly one sees patients endure for two or three years and sometimes for a decade, or, in the rarest reported instances, over twenty years. In the case reported previously by the author, as being wholly symptom-free and normal as to blood-picture, death occurred from wholly unrelated causes. This patient when seen after a period of seven years showed most robust health.

It is most important that one hold in mind constantly the tendency to remission commonly attending this ailment and the readiness with which the greater number respond to rational treatment.

The author's experience has convinced him that in many, if not most, instances a too hurried resort to transfusion is fraught with danger to the patient and may shorten rather than lengthen the duration of a remission and abridge his after-lifetime. One must bear in mind also the possibility and frequency of repeated remissions even in very advanced cases.

Needless to say, the availability of facilities for treatment is an important factor. In no disease is rest, proper feeding, and carefully supervised resumption of physical and mental activity more important.

Pathology.—The autopsy findings in Addisonian pernicious anemia disclose certain striking pathologic changes indicative for the most part of the high grade of hemolysis present in this disease, together with the extreme grade of anemia present and its long duration. They throw little light upon the actual cause of the disease.

Fatty degeneration is the dominant process in the parenchymatous viscera and is especially marked in the liver, heart and kidneys. The heart is usually dilated and flabby and contains little or no blood. Its color is a pale yellow.

The *red bone marrow* is strikingly deepened in color and the yellow marrow of the long bones appears to be transformed into a deep red gelatinous substance often likened to currant jelly. This appearance is usually more striking than that seen in even the severest forms of secondary anemia.

An extraordinarily large deposit of iron in the liver and to a lesser degree in the spleen and kidneys attends the continued destruction of red cells. A section of the liver thoroughly treated with a weak solution of ferrocyanid of iron and then washed in a weak aqueous solution of hydrochloric acid assumes a strikingly beautiful blue color.

The stomach and intestines are described usually as either plainly atrophic or normal in appearance. It is claimed by certain observers that the atrophic changes are in large measure only apparent and due to postmortem change.

Favor and Bloch maintain that they are not to be found if the abdomen is injected with formalin at once after the death of the patient. This observation is confirmed by Gulland and Goodall. Hemolymph glands of a deep red color may be present in large numbers especially along the anterior surface of the lumbar portion of the spine. The kidneys show an excess of iron content and are usually the seat of some organic change. The entire general picture presented by the victim on postmortem section is one of extreme anemia and deficient blood volume. Even the imperfectly formed blood-clots show a pallid red. The changes encountered in the brain and spinal cord in this type of anemia are described under "Nervous and Mental Symptoms," page 813.

HEMOLYTIC ANEMIAS

(Other Than Addisonian Pernicious Anemia)

The group of anemias in which hemolysis enters in some degree into the blood-picture is a large one. In some instances hemolysis is the dominant factor and the picture may closely resemble that of Addisonian pernicious anemia, whereas in others the evidences of hemolysis are comparatively slight. Similarly the pathologic changes in connection with anemias of this type may be such as show a decided involvement of the bone marrow, whereas in others this factor may be almost wholly indeterminable. The cases constituting this group may be acute or chronic, primary or secondary, and necessarily must show the widest divergence in etiology, gravity and general symptomatology.

They may be febrile or afebrile, and the spleen may be demonstrable, greatly enlarged, or so slightly affected as to show little or no change on palpation. In the severer cases the color index may be high, but in the greater number it is normal or even slightly lowered, and the red cells are never markedly achromic.

With respect to the outward appearance of such patients, it may be said that the skin and scleræ show almost invariably some evidences of the hemolytic type of jaundice, but the degree to which this is manifest varies within wide limits. In short, the condition is an extremely common one in its association with many chronic diseases, especially such as are septic, carcinomatous or malarial in type, and must vary from the extreme grades seen occasionally in dibothriocephalus intoxication, or in cases of gastric carcinoma with sepsis and metastases, in which the picture closely resembles that of Addisonian pernicious anemia, to the many cases associated with mild sepsis resulting from chronic focal infections.

Even in graver cases the color index is seldom as high as in the Addisonian anemia, and may be definitely low. Anisocytosis may be marked but the smaller types seem to dominate the field and normoblasts and microblasts usually constitute a majority of any erythroblasts present.

Dibothriocephalus Anemia.—The more severe cases of anemia resulting from the disintegration of this intestinal parasite within the body more closely resemble the Addisonian pernicious anemia than almost any others and are extremely likely to lead to errors in diagnosis.

It is particularly important that this statement be noted, because of the fact that the outward appearance of such patients so closely resembles that of the victim of Addisonian pernicious anemia in the more extreme instances. There is much the same coloring of the integument and the blood-picture itself may show but very slight variation from that of the Addisonian pernicious type. Occasionally the color index is definitely high, though in most such cases this finding is not present.

In connection with the blood itself, however, it should be noted that, although the count may be extremely low, marked chromatophilia is seldom seen, and though there may be a marked variation in the size of the red cells present the predominance of the macrocyte amongst the abnormal forms, so characteristic of advanced pernicious anemia, is not seen in these cases which so closely simulate it.

This particular form of anemia is relatively rare in this country though comparatively common in regions like Finland and in other countries where fish compose a main article of diet and in which the *dibothriocephalus latus* is more or less prevalent as a parasite.

It is an interesting fact that, although there are many other parasites which may infect the human body and produce anemia, this particular one under discussion is essentially the only one producing this extreme hemolytic type of blood change.

In any case presenting the outward appearance of Addisonian pernicious anemia but showing such discrepancies in the blood-picture as are set forth in this article, the question of dibothriocephalus intoxication should be considered carefully in the absence of any proof of an extreme grade of gastric carcinoma with sepsis and metastases. Positive diagnosis in the case of dibothriocephalus anemia must depend, of course, upon the finding of the proglottids or the ova in the stools of the suspect.

The Hemolytic Anemia of Pregnancy.—The literature with respect to the occurrence of a high grade of hemolytic anemia during the latter part of pregnancy or subsequent to delivery is greatly confused and it is impossible to elicit a clear picture which would satisfy one that the condition of pregnancy in itself is the causative factor.

This statement may be made with especial emphasis with relation to the cases following delivery in which the element of concealed sepsis might be supposed to play an important part if not the dominant rôle. Furthermore, one has to consider the question of posthemorrhagic anemias of a severe type in this connection. On the other hand the possibility that anemias of a severe type may develop by reason of the state of pregnancy itself must be admitted.

It is essential at all events to bear in mind the fact that, although any anemia occurring during pregnancy is usually of the mild grade and a comparatively unimportant finding, nevertheless cases of the most severe grade and occasionally running to a fatal issue may be encountered. In some of these the spleen is markedly enlarged; in others it is but little affected.

With respect to the blood findings and the outward appearance of the patient, it may be said that in certain instances both the color of the skin and the blood-picture itself may be almost indistinguishable from the findings in Addisonian pernicious anemia, and cases are reported showing a high color index, diminished blood-platelets, a low leukocyte count, and considerable anisocytosis, poikilocytosis and polychromatophilia. In such cases, however, as in the *dibothriocephalus latus* anemias, the dominance of the macrocyte amongst the abnormal forms is very rarely observed.

Acute Hemolytic Anemia.—Cases are reported by various observers of an anemia of a profound hemolytic type developing with extraordinary rapidity so that in a few days the red blood count may have dropped below 1,000,000 cells per cubic millimeter. In the cases reported its association has been with an acute sepsis in most instances, although scarlet fever has also given rise to the same condition. Sepsis following child-birth or abortion plays perhaps the larger part in the reports so far made. In such cases anisocytosis may be very marked; the dominance of the macrocyte, so characteristic of chronic Addisonian pernicious anemia, may be noted; and the color index usually is high.

On the other hand the number of granular leukocytes is increased, as are the blood-platelets. In some instances there seems to have been noted a large increase in the phagocytic endothelial leukocytes. Among the many causes capable of producing an anemia of the acute hemolytic type one may mention malignant endocarditis, pneumonia, and poisoning by certain chemicals such as acetanilid, trinitrotoluol, anilin, nitrobenzol, and many other members of the coal-tar group. Certain anemias of this acute hemolytic type were described by Laube and Arneth under the term "leukanemia" which now has been discarded wholly.

BIBLIOGRAPHY

Chlorosis

Allbutt, Sir C. In Allbutt and Rolleston, System of Medicine, 1919, Vol. V, 681.
Armbrust. Jour. de Physiotherapie, July 15, 1909.
Arneth, J. Diagnose u. Therapie der Anamien, A. Stuber, Wurzburg, 1907, pp. 140 and 164.
Ash, J. E. Arch. Int. Med., 1914, xiv, 8.
Barker, L. F. In Monographic Medicine, Vol. III, p. 195, D. Appleton & Co., N. Y.
Cabot, R. C. Osler & McCrae's Modern Medicine, 1915, 2nd ed., Vol. IV, 619, D. Appleton & Co., New York.
Dickinson. N. Y. Med. Record, Sept. 3, 1910.
Di Poggio, E. Riv. Med., Milano, 1919, xxvii, 125.
Ehrlich, P. et al. Diseases of the blood. Nothnagel's Encyclopedia of Practical Medicine, Translated by A. Stengel, 1905.
Ferreira. La presse médicale, Nov. 7, 1908. Gazz. degli Osped., Aug 12, 1909. Arch. Mal du Coeur, Dec. 19, 1910.
Finkelstein, H. Berl. klin. Wchnschr., 1911, xlviii, 1829.
Glaevecke. Arch. f. exper. Path. u. Pharm., 1883.
Greene, C. L. Medical Diagnosis, 4th Ed., pp. 143 and 147, P. Blakiston's Son & Co., Phila.
Gulland, G. L., and Goodall, A. The blood. 2nd ed., 1914, W. Green & Sons, Edinburgh & London.
Haldane, J., and Smith, J. L. Jour. Physiol., 1899-1900, xxv, 331.
Hooper, C. W., Robscheit, F. S., and Whipple, G. H. Amer. Jour. Physiol., Sept. 1920, liii, pp. 151, 236 and 263.
Huchard et Fiessinger. Jour. des Praticiens, 1908, 41 and 42.
Lüders, C. Med. klin. Berlin, 1920, xvi, 40.
Martin, C. F. In Forchheimer's Therapeusis of Internal Diseases, Vol. III, p. 811, D. Appleton & Co., New York.
Mayer, E. Ergeb. der Physiol., 1906, v.
Morawitz, P. München. Med. Wchnschr., 1910, lvii, 1425.
Naegeli, O. Blutkrankheiten u. Blutdiagnostik, 1912.
Neusser, E. v. Wien. klin. Wchnschr., 1913, xxvi, 1526.
Osler, Sir W. Practice of Medicine, 8th Ed., p. 730, D. Appleton & Co., New York.
Piccinimi. Folia Hæmatology, 1907, i.
Plesch, J. Ztschr. f. exper. Pathol. u. Therap., 1909, vi, 380.
Provinziali. Synop., Folia Hæmatology, April, 1910.
Schwartz, H., and Rosenthal, N. Arch. Pediatrics, Jan., 1920, xxxvii, 1.
Salkowski. Berlin. klin. Wchnschr., 1908, iv.
Smith, J. Trans. Path. Soc. London, 1900, li, 311.
Stockman. Brit. Med. Jour., 1893, i, 881, 942. Edin. Med. Jour., 1895, xli, 413. Brit. Med. Jour., 1895, ii, 1473. Brit. Med. Jour., 1896, i, 1077.
Von Jagic, N. Med. Klinik, 1915, ii, 69.
Von Noorden. In Nothnagel's Spec. Path. u. Therap., 1897, Vol. VIII, ii, Edited by Stengel, Eng. Edition, 1905.
Virchow. Ueber die Chlorosen u. Anomalien im Gefäss-apparate, Berlin, 1872.
Wandel. Deut. Arch. f. klin. Med., xc, 1 u. 2.
Ward, G. R. Clinical Hæmatology, 1914.

Aplastic Anemia

Accolas, G. L'anémie pernicieuse aplastique. Thèse de Lyon, 1910, Imprimeries réunies, 8 Rue Rachais.
Archibald, A. Med. Clinics of North America, November, 1919, iii, 757.
Barker, L. F. Monographic Medicine, Vol. III, 200, D. Appleton & Co., New York.
Bernardi, G. Riforma med., July 26, 1919, xxxv, 617.
Boycott, A. E., and Douglas, C. G. Jour. Path. and Bact., 1908-09, xiii, 256.
Cabot, R. C. Osler's Modern Medicine, 1st ed., 1908, Vol. IV, D. Appleton & Co., N. Y.
Comby, J. Arch. de méd. d. enf., October, 1919, xxii, 545.
Ehrlich, P. Charité-Ann., 1888, xiii, 300.
Glenn, R. A., and McVey, C. L. Northwest Medicine, April, 1919, xviii, 65.

Gorke, H. München. med. Wchnschr., Oct. 22, 1920, lxvii, 1226; abstr. J. A. M. A., Feb. 26, 1921, lxxvi, 625.

Greene, C. L. Medical diagnosis, 4th ed., p. 151, P. Blakiston's Son & Co., Phila., Pa.

Herz, A. Wien. klin. Wchnschr., 1908, xxi, 1363.

Hirschfeld, H. Folia Hæmatology, Leipzig, 1911, xii, 347.

Hurwitz, S. H., and Drinker, C. K. Jour. Exper. Med., 1915, xxi, 401.

Kleinschmidt, H. Jahrb. f. Kinderh., Berlin, 1915, n. s. lxxxi, 1-16.

Krumbhaar, E. B. Jour. A. M. A., 1919, lxxii, 39.

Larrabee, R. C. Jour. A. M. A., Dec. 11, 1920, lxxv, 1632.

Lee, R. I., and Minot, G. R. Cleveland Med. Jour., 1917, xvi, 65.

Minot, G. R. Arch. Int. Med., 1917, xix, 1062. Amer. Jour. Med. Sci., 1916, clii, 48. Oxford Medicine, Vol. II, 605.

Musser, J. H., Jr. Arch. Int. Med., 1914, xiv, 275. Med. Clin. of North America, Philadelphia, 1919-20, iii, 1403.

O'Malley, J. J., and Conrad, H. B. Jour. A. M. A., 1919, lxxiii, 1761.

Parkinson, J. P. Proc. Royal Soc. Med., London, 1918-19, xii, Section Stud. Dis. Children, pp. 72 and 110. British Jour. Child. Dis., Jan.-March, 1919, xvi, 1.

Rennie, G. E. Med. Jour. Australia, June 14, 1919, 1, 485.

Schilling-Torgau, V Beiheft z. Arch. f. Schiffs- u. Tropen. Hyg., Leipzig, 1912, xvi, 448.

Schneider, J. P. Amer. Jour. Med. Sci., 1918, clvi, 799.

Selling, L. Johns Hopkins Hosp. Rep., 1913, xvii, No. 2, p. 83. Bull. Johns Hopkins Hosp., 1910, xxi, 33.

Smith, L. W. Amer. Jour. Dis. of Children, 1919, xvii, 174.

Weber, F. P. Proc. Roy. Soc. Med., London, 1913-14, vii, Med. Sect., 179. Folia Hæmatology, Leipzig, 1914, xix, (Arch.) 15-24.

Myelophthisic Anemia

Jack, W. R., and Teacher, J. H. Glasgow Med. Jour., 1910, lxxxix, 81.

Minot, G. R. Oxford Medicine, Vol. II, 603.

Addisonian Pernicious Anemia

Adami, J. G. Jour. A. M. A., 1899, xxxiii, 1509-1514; and 1572-1576.

Addis, T. Arch. Int. Med., 1915, xv, 414.

Addison. On the constitutional and local effects of disease of the suprarenal capsules, 1855; republished in Addison's Complete Works, New Sydenham Soc., 1868, 211.

Addison, T. London Med. Gaz., 1849, xliii, 517.

Adler, H. M. Jour. Med. Research, Boston, 1913, xxviii, 199.

Archibald, A. St. Paul Med. Jour., 1917, xix, 43.

Barker, L. F. Monographic Medicine, 1916, Vol. III, D. Appleton & Co., New York.

Barnes, F. M., Jr. Jour. Missouri Med. Assn., St. Louis, 1913-14, x, 452.

Barrett, A. M. Amer. J. Insanity, Baltimore, 1912-13, lxix, 1063.

Bartlett, C. J. Jour. A. M. A., 1913, lx, 176.

Benedict, F. G., et al. Monograph No. 280 of the Carnegie Institution of Washington, 1919.

Bielonovsky. Thèse de Saint Petersburg, 1902.

Biermer. Correspondenzblatt f. schweizer Aertze, 1872, ii, 15.

Blankenhorn, M. A. Arch. Int. Med., 1917, xix, 344.

Bloch. Thèse de Paris, 1908.

Bloomfield, A. Bull. Johns Hopkins Hosp., 1918, xxix, 101.

Bloor, W. R., and Macpherson, D. J. Jour. Biol. Chem., 1917, xxxi, 79.

Boggs, T. R. Johns Hopkins Hosp. Bull., Baltimore, 1913, xxiv, 322.

Bordet. Ann. de l'Inst. Pasteur, 1900.

Borries, G. V. T. Hospitalstidende (Copenhagen), 1915, lxviii, 1015.

Bramwell, B. British Med. Jour., 1909, i, 209; 1911, i, 547; and June 22, 1912.

Briggs, LeR. H. Amer. Jour. Med. Sc., 1914, cxlviii, 413.

Bunting, C. H. Jour. A. M. A., 1907, xlix, 476. Jour. Exper. Med., 1906, viii, 625.

Burch. Jour. A. M. A., March, 13, 1909.

Butler, G. G. Quart. Jour. Med., 1913, vi, 145.

Cabot, R. C. Amer. Jour. Med. Sc., Phila. and N. Y., 1900, cxx, 139. Pernicious and secondary anemia, chlorosis, and leukemia. Osler and McCrae's Modern Medicine, 1915, Vol. IV, 619, D. Appleton & Co., New York.

Cabot, R. C., and Richardson, O. Jour. A. M. A., 1919, lxxii, 991.

Capps, J. A. Jour. Med. Res., 1903-04, x, 367.

Carr, J. G. Amer. Jour. Med. Sci., Nov., 1920, clx, 737.

Carre, H., et Vallee. Annals de l'Instit. Pasteur, 1916, xxx, 383.

Cederburg, A. Berliner klin. Wchnschr., 1914, li, 585.

Charlton, W. Therap. Halbmonatsh., Feb. 15, 1920, xxxiv, 111; abstr. Jour. A. M. A., July 24, 1920, lxxv, 280.

Chauffard, A., and Bernard, M. Presse méd., July 3, 1919, xxvii, 361; abstr. Jour. A. M. A., Aug. 23, 1919, lxxiii, 647.

Christian, H. A. Arch. Int. Med., 1916, xviii, 429.

Decastello, A. Deutsche med. Wchnschr., Leipzig u. Berlin, 1914, xl, 639 and 692.

Decastello, A., and Kijukoff, A. Med. Clin., 1911, vii, 225, and 267.

Dejerine, J., et Mouzon, J. Rev. Neurol., Paris, 1914, xxii, 206.

D'Espine, A. Rec. méd. de la Suisse Romande, 1918, xxxviii, 461.

DeSchweinitz, G. A. Trans. Am. Ophthal. Society, 1896.

Dill. Proc. Roy. Soc. Med., ii, Clin. 21, p. 2.

Drinker, C. K., and Hurwitz, S. H. Arch. Int. Med., 1915, xv, 733.

Eason, J. Edinburgh Med. Jour., Dec., 1920, xxv, 389.

Emerson, C. P. Clinical diagnosis, 1911.

Engel. Ztschr, f. klin. Med., 1904, liv, 154.

Eppinger, H. Berliner klin. Wchnschr., 1913, l, 1509, 1572, 2409.

Ewald, C. A., and Friedberger, E. Deutsche med. Wchnschr., 1913, xxxix, 1293 and 1449.

Faber, A. Ugeskrift f. Læger, 1917, lxxix, 409; abstracted in Jour. A. M. A., 1917, lxviii, 1590.

Faust, E. S., and Tallquist, T. W. Arch. f. Exper. Path. u. Pharm., 1907, lvii, 366.

Ferrata, A. L. Emopatie. Soc. Ed. Lib., 1918.

Flesch, H. Ergebn. d. inn. Med., Berlin, 1909, iii, 186.

Fowler. Medical reports on the internal use of arsenic, London, 1786.

French, H. In Allbutt and Rolleston's System of Medicine, 1909, Vol. V, 727.

Friedenwald, J., and Morrison, T. H. Jour. A. M. A., 1919, lxxiii, 407.

Gettler, A. O., and Lindeman, E. Arch. Int. Mel., Oct. 1920, xxvi, 453.

Giffin, H. Z., and others. Amer. Jour. Med. Sc., 1918, clv, 562.

Giffin, H. Z., and Sanford, A. H. Amer. Jour. Med. Sc., 1918, clv, 562.

Gilbert, and Weil. Arch. Mal. du Coeur, 1908, 553.

Grawitz, E. Deutsch. med. Wchnschr., 1904, 1092 and 1135. Klin. Pathologue des Blutes, 4 Aufl., 1911.

Greene, C. L. Medical diagnosis, 4th Ed., p. 148, P. Blakiston's Son & Co., Phila., Pa.

Guillain, G. Monde méd., Paris, 1914, xxiv, 353.

Gunn. Brit. Med. Jour., July 18, 1908.

Gunn and Feltham. Brit. Med. Jour., Jan. 21, 1911.

Hamman, L. N. Y. State Jour. Med., Dec., 1919, xix, 420.

Hannema, L. S. Nederlandsch. Tijdschrift. Voor Geneeskunde, 1917, ii, 1653.

Hansmann, G. H., and Howard, C. P. Jour. A. M. A., Oct. 25, 1919, lxxiii, 1262.

Hewlett, A. W. Monographic Medicine, 1916, Vol. I, D. Appleton & Co., New York.

Hill, L. W. Arch. Int. Med., 1915, xvi, 809.

Hoover, C. F. Cleveland Med. Jour., 1918, xviii, 143.

Houston, T. Brit. Med. Jour., 1902, 1, 1464.

Hunter, W. The Practitioner, London, 1888, xli, 81. British Med. Jour., 1907, ii, 1299. Severest anemias; their infectious nature, diagnosis and treatment. Macmillan & Co., London, 1909.

Iwao, T. Biochem. Zeitschrift, 1914, lix, 436.

Jones, B. L., and Raphael, T. Arch. Neurol. and Psychiat., July, 1920, iv, 55.

Kahn, M., and Barsky, J. Arch. Int. Med., 1919, xxiii, 334.

King, J. H. Arch. Int. Med., 1914, xiv, 145.

Kipp, H. A. Jour. Biol. Chem., Sept., 1920, xliii, 413.

Klemperer. Berlin. klin. Wchnschr., No. 52, 1908.

Konnecke, W. Deutsch. Arch. f. klin. Med., 1914, cxv, 177.

Krumbhaar, E. B. Amer. Jour. Med. Sc., 1915, cl, 227.

Laache, S. Die Anaemie, Christiana, 1883.

Lazarus, A. Klinik der Anämien, 2 Aufl., Wien und Leipzig, 1913, A. Hölder.

Lee, R. L., Minot, G. R., and Vincent, B. Jour. A. M. A., 1916, lxvii, 719.

Lee, R. L., Vincent, B., and Robertson, O. H. Jour. A. M. A., 1915, xv, 216.

Leebe. München. med. Wchnschr., 1911, lviii, 1184.

Lefevre. Thèse de Paris, 1907.

Lichtheim. Zur Kenntniss d. Perniciösen Anäemia, VI, Congress f. innere Med., 1887, vi, 84.

Lindeman, E. Jour. A. M. A., 1918, lxx, 1292, and 1209.

Lundsgaard, C. Jour. Biol. Chem., 1918, xxxiii, 133. Jour. Exper. Med., 1918, xxvii, 179.

Lurie, L. A. Arch. Neurol. and Psychiat., July, 1919, ii, 67.

McCaskey, G. W. N. Y. Med. Jour., 1913, xcvii, 67.

McCrudden, F. H. Boston Med. and Surg. Jour., 1917, clxxvii, 907.

McNeil, C. Jour. Path. and Bact., 1911, xv, 56.

McPhedran, W. F. Jour. Exper. Med., Lancaster, Pa., 1913, xviii, 527.

Macora, F. Policlinico (sez. med.), Nov., 1919, xxvi, 424; abstr. Jour. A. M. A., Feb. 14, 1920, lxxiv, 496.

Martin, C. F. In Forchheimer's Therapeusis of Internal Disease, Vol. III, 824, D. Appleton & Co., New York.

Martius, F. W. A. Achylia gastrica, ihre Ursachen und ihre Folgen; mit einem anatomischen Beitrag von O. Lubarsch. 1897. F. Deuticke, Leipzig u. Wein.

Masing, E. St. Petersburg med. Wchnschr., 1909, xxxiv, 497.

Mathes, M. Kong. f. inn. Med., 1913, xxx, 290.

May, E. Arch. Mal. du Coeur, 1914, vii, 123.

Mensi, E. Pediatria, Sept. 1, 1920, xxviii, 785; abstr. J. A. M. A., Nov. 6, 1920, lxxv, 1298.

Meulengracht, E. Ugesk. f. Læger, June 17, 1920, lxxxii, 777; abstr. Jour. A. M. A., Aug. 28, 1920, lxxv, 644.

Minot, G. R. Nitrogen metabolism before and after splenectomy in a case of pernicious anemia. Johns Hopkins Hosp. Bull., 1914, xxv, 338. Clinics of North America, 1918, 1, 1103. Oxford Medicine, Vol. II, 589.

Minot, G. R., and Denny, G. P., and Davis, D. Arch. Int. Med., 1916, xvii, 101.

Minot, G. R., and Lee, R. L. Boston Med. and Surg. Jour., 1917, clxxvii, 761.

Moffitt, H. C. Amer. Jour. Med. Sc., 1914, cxlviii, 817. Boston Med. and Surg. Jour., 1914, clxxi, 289.

Morawitz, P. Handb. d. inn. Med. (Mohr & Staehelin), 1912, iv, 174.

Mosenthal, H. O. Arch. Int. Med., 1915, xvi, 733.

Muir, R., and Dunn, J. S. Jour. Path. and Bact., Cambridge, 1914-15, xix, 417.

Naegeli, O. Blutkrankheiten u. Blutdiagnostik, Leipzig, 1912.

Newcomer, H. S. Jour. Biol. Chem., 1919, xxxvii, 465.

Osler, Sir W. Practice of Medicine, 8th Ed., p. 733, D. Appleton & Co., New York.

Patek, A. J. Jour. A. M. A., 1911, lvi, 1315.

Patton, J. M. Internat. Clinics, 1918, iv, 15.

Penrose, C. A. South. Med. Jour., 1915, viii, 879.

Pepper, W. Amer. Jour. Med. Sc., Philadelphia, 1875, n. s. lxx, 313.

Peters, A. W., and Rubnitz, A. S. Arch. Int. Med., Nov., 1920, xxvi, 561.

Pfeiffer, J. A. F. Jour. Nerv. and Mental Dis., N. Y., 1915, xlii, 75.

Piot. Thèse de Lyon, 1908.

Quincke. Volkmann's Sammlung, 1876, 100. Deutsch. Arch. f. klin. Med., 1877, xx, 1.

Robertson, O. H. Arch. Int. Med., 1915, xvi, 652, and 429. Arch. Int. Med., 1915, xv, 1072. Jour. Exper. Med., 1917, xxvi, 221.

Robertson, O. H., and Rous, P. Jour. Exper. Med., 1917, xxv, 665.

Rous, P. Jour. Exper. Med., 1918, xxviii, 645.

Rous, P., and Robertson, O. H. Jour. Exper. Med., 1917, xxv, 651.

Schauman, O. Samml. klin. Vortr., Leipzig,: 1900, Nr. 287 (Innere Med., Nr. 84), 231. Deutsch. med. Wchnschr., 1912, xxviii, 1228.

Schneider, J. P. Arch. Int. Med., 1916, xvii, 32. Arch. Int. Med., 1917, xix, 156. Jour. A. M. A., June 26, 1920, lxxiv, 1759.

Sellards, A. W. Jour. Med. Research, 1918, xxxviii, 293.

Sellards, A. W., and Minot, G. R. Jour. Med. Research, 1916, xxxiv, 469.

Seyderhelm, R. Arch. f. Exper. Path. u. Pharm., 1918, lxxxii, 253.

Signorelli, E. Riforma med., July 10, 1920, xxxvi, 624; abstr. Jour. A. M. A., Sept. 25, 1920, lxxv, 903.

Silbermann, S. Med. Klinik., Feb. 15, 1920, xvi, 183.

Smith, T. Jour. Med. Research, Boston, 1904, xii, 385.

Speidel, W. C., and others. Northwest Medicine, April, 1920, xix, 94.

Spengler, G. Wien. klin. Wchnschr., Jan. 22, 1920, xxxiii, 86; abstr. Jour. A. M. A., June 26, 1920, lxxv, 1805.

Squier, T. L. Jour. Lab. and Clin. Med., 1916-17, ii, 552.

Stern, H. Arch. Diagnosis, N. Y., 1913, vi, 326.

Stettner, E. Jahr. f. Kinderh., Berlin, 1914, n. F. lxxx, 467.

Stockman, R. Brit. Med. Jour., 1895, ii, 1473.

Stockton, C. G. Amer. Jour. Med. Sci., Oct., 1919, clviii, 471.

Syllaba, L. Arch. gén. de Méd., Paris, 1904, xii, 2369.

Tallqyist, T. W. Ztschr. f. klin. Med., 1917, lxi, 427.

Taylor, E. W., and Putnam, J. J. Jour. Nerv. and Ment. Dis., 1901, xxviii, 1074.

Tormey, A. W. Wisconsin Med. Jour., Dec., 1920, xix, 348.

Van Slyke, D. D. Jour. Biol. Chem., 1918, xxxiii, 127.

Vaugeon. Thèse de Paris, 1902.

Vogel, K. M. Jour. A. M. A., 1916, lxvi, 1012.

Wanner. Schweiz. med. Wchnschr., Aug. 5, 1920, 1, 685; abstr. Jour. A. M. A. Oct. 9, 1920, lxxv, 1030.

Ward, G. Practitioner, Feb., 1920, civ, 145.

Whipple, G., and Hoover, C. Amer. Jour. Physiol., 1916, xl, 349; 1917, xlii, 544; 1917, xliii, 258; and 1917, xliii, 275.

White, W. H. Proc. Roy. Soc. Med., London, 1912-13, vi, Clin. Sect., 165.

Wilbur, R. L., and Addis, T. Arch. Int. Med., 1914, xii, 235.

Williamson, C. S. Med. Clinics of North America, May, 1920, iii, 1581.

Zadek, J. München. med. Wchnschr., Aug. 13, 1920, lxvii, 960. Deutsche med. Wchnschr., Oct. 9, 1919, xlv, 1133; abstr. Jour. A. M. A., Feb. 7, 1920, lxxiv, 431.

Woltmann, H. W. Amer. Jour. Med. Sc., 1919, clvii, 400. Arch. Int. Med., 1918, xxi, 791.

Hemolytic Anemias

Barker, L. F. Monographic Medicine, Vol. III, 188, D. Appleton & Co., New York.

Biermer, A. Fettige Degeneration des Herzens und der Gefässe in Folge von idiopathischer und Secundärer Anämie. 42. Versamml. Deutsch. Naturf. u. Aerzte, Dresden, 1868.

Bishop, F. W. Arch. Int. Med., 1914, xiv, 388.

Bizzarri, A. Hæmatologica, Napoli, 1920, i, 141.

Channing, W. N. E. Quart. Jour. Med. and Surg., 1842-43, i, 157.

Clark, H. M., and Evans, F. A. Bull. Johns Hopkins Hosp., 1920, xxxi, 354.

Esch, P. Ztschr. f. Geburt. u. Gyn., 1916, lxxix, l.

Faust, E. S., und Tallqvist, T. W. Arch. f. exper. Pathol. u. Pharm., Leipzig, 1907, lvii, 366.

Gasbarrini, A. Policlinico, 1915, xxii, 1537.

Gram, H. C. Ugesk f. Læger., Dec. 23, 1920, lxxxii, 1609; abstr. Jour. A. M. A., March 5, 1921, lxxvi, 692.

Greene, C. L. Medical diagnosis, 4th Ed., p. 143, P. Blakiston's Son & Co., Phila., Pa.

Gusserow, A. Arch. f. Gynäk., 1871, ii, 218.

Hamilton, A. Bull. U. S. Bureau of Labor Statistics, 1917, No. 219.

Hess, L., und Muller, H. Wien. klin. Wchnschr., 1913, xxvi, 1833.

Hopkins, J. G. Arch. Int. Med., 1910, vi, 270.

Joanivics, G., und Pick, E. P. Ztschr. f. exper. Path. u. Therap., 1909-10, vii, 185.

Kozitschek, H. Wien. Med. Wchnschr., 1920, lxx, 389.

Lepage, G. Arch. Mal. du Coeur, 1914, vii, 558.

Martin, C. F. *In* Forchheimer's Therap. of Internal Diseases, Vol. III, 808, D. Appleton & Co., New York.

Martin, T. R. Jour. Lancet, 1919, xxxvii, 303.

Marxer, A. Zeit. f. Immunit. u. exper. Therap., Jena, 1920, xxix, 1-10.

Minot, G. R. Oxford Medicine, Vol. II, 636. Jour. Indust. Hygiene, 1919, i, 301.

Morusset, Mouriquand, E., et Thevenot. La Semaine méd., 1907, xxvii, 602.

Osler, Sir W. Practice of Medicine, 8th Ed., p. 728, D. Appleton & Co., New York. Brit. Med. Jour., Jan. 4, 1919, 1, 1.

Pearce, R. M., Krumbhaar, E. B., and Frazier, C. H. The spleen and anemia. Philadelphia, 1918.

Pittaluga, G. Archives Españoles de Pediatria, 1918, ii, 513.

Pontano, T. Policlinico, 1912, Sez. Prat., xix, p. 3.

Rideau, Dumas, L., et Poisot. La Presse méd., 1907, xv, 370.

Rieux, J. Rev. de Méd., Oct., 1920, xxxvii, 505.

Rowley, M. W. Jour. Exper. Med., 1908, x, 78.

Schapiro, H. Ztschr. f. klin. Med., Berlin, 1887, xiii, 416.

Schaumann, O. Zur Kenntniss der sogenannten Bothriocephalus-Anämie. Helsingfors, 1894, Weilim & Goos. Die perniciöse Anämie im Lichte der modernen Gifthypothese. Samml. klin. Vortr., Leipzig, 1900, Nr. 287, p. 231.

Schmidt, H. D. Surg., Gyn., and Obstet., 1918, xxvii, 596. Jour. Mich. Med. Soc., March, 1921, xx, 92.

Schupbach, A. Cor.-Bl. f. schweizer Aerzte, 1914, xliii, 1535.

Sonder, F. E. Bull. of Lying-in Hosp., N. Y., 1906-07, iii, 27.

Stengel, A., and White, C. Y. Contrib. of the Wm. Pepper Lab. of Clin. Med., 1903.

Tallqvist, T. W. Ztschr. f. klin. Med., Berlin, 1907, lxi, 427. Über experimentelle Blutgift-Anämien. Helsingfors, Helsingfors Centraldr., 1899.

Teeter, C. E. Jour. A. M. A., 1907, xlviii, 608.

Thompson, W. G. Med. News, Philadelphia, 1905, lxxxvi, 635.

Van Nuys, F. Boston Med. and Surg. Jour., 1907, clvi, 390.

Wolff, A. Deutsch. med. Wchnschr., 1914, xl, 643.

Treatment of Anemia

Armbrust, A. Jour. d. Physiotherapie, 1909, vii, 331.

Barker, L. F., and Sprunt, T. P. Jour. A. M. A., 1917, lxix, 1919.

Bloch, L. Action de l'Arsenic sur le Sang et les Organes Hémopoïetiques. Thèse de Paris, 1908.

Bramwell, B. Clinical Studies, 1902; Oct., 1906; and 1908-9, vii, 154. Brit. Med. Jour., 1909, i, 209; 1913, ii, 1093, and 2734; 1911, i, 547; June 22, 1912, p. 1413.

Cantacuzene. Ann de l'Inst. Pasteur, June, 1920.

Courmont et Andre. Jour. de Phys. et Path. Gen., Jan., 1904. Folia Hæmatology, 1904, 389. Ann. de l'Inst. Pasteur, June, 1900.

Croftan. Jour. A. M. A., Aug. 13, 1910.

David, O. Deutsch. Arch. f. klin. Med., 1912-13, cix, 129.

Fowler. Medical reports on the internal use of arsenic. London, 1786.

Grawitz, E. Deutsch. med. Wchnschr., 1904, pp. 1091 and 1135.

Gunn. Brit. Med. Jour., July 18, 1908.

Gunn, and Feltham. Brit. Med. Jour., Jan. 21, 1911.

Heinrich. Therap. Monatschrift, Nov., 1910, 593.

Klemperer. Berlin, klin. Wchnschr., No. 52, 1908.

Lefevre. Thèse de Paris, 1907.

Metchnikoff et Besredka. Ann. de l'Inst. Pasteur, June, 1900.

Meyer, A. L., and Dubois, E. F. Arch. Int. Med., 1916, xvii, 965.

Minot, G. R. Bull. Johns Hopkins Hospital, 1914, xxv, 338.

Mosenthal, H. O. Bull. Johns Hopkins Hospital, 1918, xxix, 129.

Musser, J. H., Jr. Boston Med. and Surg. Jour., 1912, clxvi, 775.

Neisser. Deutsch. med. Wchnschr., 1908, xxxv.

Norso, P. Synop., Folia Hæmat., 1907, i.

Pribam. Biochem. Ztschr., 1906, i.

Reicher, K. Berlin klin. Wchnschr., Oct. 12 and 19, 1908.

Rosenquist, E. Zeitschr. f. klin. Med., 1903, xlix, 193.

Stockman, R., and Chateris, F. J. Jour. Path. and Bact., 1903, vii, 443.

Strauss, H. Von Noorden's Metabolism and practical medicine, English Trans., Chicago, 1907, Vol. II, 350.

Vaugeon. Thèse de Paris, 1902.

Vetlesen. Nordsk. Mag. for Lægvid., 1908, 1152; synop. in Folia Hæmat., April, 1910. Medical Review, London, 1909, xii, 157.

Von Noorden, C. Therap. Monatschrift, 1915, xxix, 293.

Whipple, G. H., and Hooper, C. W. Amer. Jour. Physiol., 1917-18, xlv, 573, 576. Arch. Int. Med., 1919, xxiii, 612, 689, 711.

Transfusion

Anders, J. M. Amer. Jour. Med. Sc., 1919, clviii, 659.

Ashby, W. Jour. Exper. Med., 1919, xxix, 267.

Bernheim, B. M. Jour. A. M. A., 1915, lxv, 1278. Blood transfusion, hemorrhage and the anemias. J. B. Lippincott Co., Phil. and Lond., 1917.

Bovaird, D. Med. Record, Feb. 11, 1911.

Brem, W. V. Jour. A. M. A., 1916, lxvii, 190.

Cahn. Synop. Folia Hæmat., April, 1910, p. 264.

Clough, M. C., and Richter, I. M. Bull. Johns Hopkins Hosp., 1918, xxix, 86.

Coca, A. F. Jour. Immunol., 1918, iii, 93.

Crile, G. W. Transfusion of blood. *In* Stereo Clinic (H. A. Kelly), Troy, N. Y., 1913, Sect. xxiv, 2-46.

Drinker, C. K., and Brittingham, H. H. Arch. Int. Med., 1919, xxiii, 133.

Duke. Jour. A. M. A., October 1, 1910.

Garbat, A. L. Jour. A. M. A., 1919, lxxii, 1.

Graham, J. M. Edinburgh Med. Jour., May, 1920, xxiv, 282.

Guillaume, A. C. Arch. Mens. d'Obstét. et Gyn., 1918, x, 217.

Halban, J. Wien. klin. Wchnschr., 1900, xiii, 545.

Hooker, R. S. Ann. of Surg., 1917, lxvi, 513.

Huber. Deutsch. med. Wchnschr., June 9, 1910.

Huck, J. G. Bull. Johns Hopkins Hospital, 1919, xxx, 63.

Hunt, E. L., and Ingleby, H. Lancet, London, June 7, 1919, 1, 975.

Jansky. Quoted by Moss, Johns Hopkins Hosp. Bull., 1910, xxi, 63; and 1911, xxii, 238.

Karsner, H. T. Jour. A. M. A., 1918, lxx, 769.

Keith, N. M., and others. Arch. Int. Med., 1915, xvi, 547.

Kimpton, A. R. Boston Med. and Surg. Jour., 1918, clxxviii, 351.

Kimpton, A. R., and Brown, J. H. J. A. M. A., 1913, lxi, 117.

Landsteiner, K., and Leiner, K. Centralbl. f. Bakteriol., 1905, I Abt. Orig., xxxviii, 548.

Lee, R. I. British Med. Jour., 1917, ii, 684.

Lewisohn, R. Surg., Gyn., and Obstet., 1915, xxi, 37. Amer. Jour. Med. Sc., 1919, clvii, 253. Ann. of Surgery, 1916, lxiv, 618.

Lindeman, E. Jour. A. M. A., 1916, lxvi, 624. Jour. A. M. A., 1914, lxiii, 1542. Jour. A. M. A., 1919, lxxii, 1661. Amer. Jour. Dis. Child., 1913, vi, 28.

Lyon, M. W., Jr. Jour. A. M. A., 1919, lxxii, 1134.

McClure, R. D. Jour. A. M. A., 1916, lxvii, 793.

McClure, R. D., and Dunn, G. R. Johns Hopkins Hosp. Bull., 1917, xxviii, 99.

McGrath, B. F. Jour. A. M. A., 1914, lxii, 1326.

Mann, G. Wiener Med. Wchnschr., 9, 1911.

Meleney, H. E., and others. Amer. Jour. Med. Sc., 1917, cliv, 733.

Minot, G. R. Boston Med. and Surg. Jour., 1916, clxxiv, 667. Oxford Medicine, Vol. II, 650. Med. Clinics of North Amer., Jan., 1920, iii, 1001.

Morawitz. Münch. med. Wchnschr., 1907, 767.

Moss, W. L. Johns Hopkins Hosp. Bull., 1910, xxi, 63; and 1811, xxii, 238. Jour. A. M. A., 1917, lxviii, 1905.

Ottenberg, R., and Happ, W. M. Jour. Exper. Med., 1920, xxi, 313.

Ottenberg, R., and Kaliski, D. J. J. A. M. A., 1913, lxi, 2138.

Ottenberg, R., and Libman, E. Amer. Jour. Med. Sc., 1915, cl, 36.

Ottenberg, R., Kaliski, D. J., and Friedman, S. S. Jour. Med. Research, 1913, xxiii, 141.

Pemberton, J. De J. Surg., Gyn., and Obstet., 1919, xxvii, 262.

Percy, N. M. Surg., Gyn., and Obstet., 1915, xxi, 360. Northwest Medicine, April, 1920, xix, 87; also May, 1920.

Peterson, E. W. Jour. A. M. A., 1916, lxvi, 1291.

Rehling and Weil. Amer. Jour. Surg., March, 1909.

Robertson, O. H., and Bock, A. V. Jour. Exper. Med., 1919, xxix, 139.

Robertson, O. H., and Rous, P. Jour. Exper. Med., 1918, xxvii, 563. British Med. Jour., 1918, i, 477.

Rous, P., and Turner, J. R. Jour. A. M. A., 1915, lxiv, 1980. Jour. Exper. Med., 1916, xxiii, 219.

Sanford, A. H. Jour. A. M. A., 1916, lxvii, 808.

Satterlee, H. S., and Hooker, R. S. Jour. A. M. A., 1916, lxvi, 618.

Scheel, O., and Bang, O. Norsk. Mag. f. Lægevidensk., March, 1920, lxxxi, 250; abstr. Jour. A. M. A., May 1, 1920, lxxiv, 1294.

Sydenstricker, V. P. W., Mason, V. R., and Rivers, T. M. Jour. A. M. A., 1917, lxviii, 1677.

Tompkins, E. H., and others. Arch. Int. Med., 1919, xxiii, 441.

Unger, L. J. Jour. A. M. A., 1917, lxix, 2159; and 1919, lxxiii, 815.

Vincent, B. Jour. A. M. A., 1918, lxx, 1219. Surg., Gyn., Obstet., 1916, xxiii, 621.

Vogel, K. M., and McCurdy, U. F. Arch. Int. Med., 1913, xii, 707.

Von Decastello, A., und Sturli, A. Münch. med. Wchnschr., 1902, xlix, 1090.

Weber. Monthly Cyclo. and Med. Bull., Dec., 1910. Deutsch. Arch. f. klin. Med., cxvii, 1, 2.

Weil, R. Jour. A. M. A., 1915, lxiv, 425.

Wright, J. H., and Minot, G. R. Jour. Exper. Med., 1917, xxvi, 395.

CHAPTER III

THE LEUKEMIAS

By Charles Lyman Greene, M.D.

Historical note, p. 833; Definition, p. 833; Etiology, p. 834; Clinical varieties, p. 834.

Chronic myeloid leukemia, p. 835; Symptomatology, p. 835:—Onset, p. 835; Outward appearance of patient, p. 835; Hemorrhage, p. 835; Lungs, p. 835; Cardiovascular system, p. 836; Heart, p. 836; Glands, p. 836; Purpura, p. 836; Leukemic retinitis, p. 836; Deafness, p. 836; Genito-urinary tract, p. 836; Metabolism, p. 836; Fever, p. 836; Nervous system, p. 836; Gastro-intestinal symptoms, p. 837; Long bones, p. 837; Spleen, p. 837; Liver, p. 837; Ascites, p. 837; Blood-picture, p. 837; Striking blood-picture, p. 838; Atypical cases of chronic myeloid leukemia, p. 838—Diagnosis of chronic myeloid leukemia, p. 839; Complications and sequelæ, p. 839; Pathology, p. 839.

Chronic lymphatic leukemia, p. 839:—Definition, p. 839; Etiology, p. 840; Symptomatology, p. 840; Diagnosis, p. 842; Complications and sequelæ, p. 842; Treatment, p. 842:—Two chief therapeutic methods, p. 842; Precautions to be observed, p. 843; Benzol, p. 843:—Disturbances with use of benzol, p. 843; Method of administering benzol, p. 843—Use of arsenic, p. 844; Tuberculin injections and use of bacterial toxins, p. 844; Splenectomy, p. 844; Control of hemorrhage, p. 844: General measures of treatment, p. 844; Prognosis, p. 845; Pathology, p. 845.

Acute myeloid leukemia, p. 846:—Course of acute myeloid leukemia, p. 846; Etiology, p. 846; Symptomatology, p. 846; Clinical types, p. 847; Treatment, p. 847; Prognosis, p. 847; Pathology, p. 847.

Acute lymphatic leukemia, p. 848:—Definition, p. 848; Etiology, p. 848; Symptomatology, p. 848; Diagnosis, p. 849; Treatment, p. 849; Prognosis, p. 849; Pathology, p. 849.

LEUKEMIA

Historical Note.—The disease was recognized first by Hughes Bennett in 1845 and his clinical description was followed by the report of Virchow in the same year. The former described it under the name of "leukocythemia" as a suppuration of the blood attended by enlargement of the spleen and liver; the latter described it under the name "leukemia" or "white blood."

Definition.—Leukemia is a morbid condition characterized by the appearance of immature leukocytes and usually by an increase in the normal leukocytes in the blood associated with a primary hyperplasia of the leukopoietic tissues, either myeloid or lymphadenoid throughout the body.*

---

* For the sake of clarity of description at least it would seem wise to cling for the present to such a definition as that given and not attempt to include cases presenting leukemic blood-pictures without associated hyperplasia of the leukopoietic tissues or those presenting the latter but lacking the blood-picture.

Two distinct forms of leukemia are recognized clinically. First, the *myeloid* type characterized by hyperplasia of the white cells of the marrow (granulocytes) and the appearance of myelocytes to the extent of from 20 to 40 per cent. of the total leukocytes present in a given specimen of blood; and second, *lymphatic* type, in which a differential leukocyte count shows a greatly increased proportion (usually 80 per cent. or more) of the leukocytes present to be lymphocytes, the dominant cell in the acute stages being, with rare exceptions, the large mononuclear form.

Etiology.—Although recent investigations have strengthened the theory that infection plays a considerable part in the production of leukemia, and certain associated microörganisms have been reported as causative, it cannot be said as yet that anything definite has been established with relation to the specific etiology of the disease. Certain workers have been successful through animal experimentation in conveying chicken leukemia from one bird to another, but no similar experiments upon men or upon the ordinary laboratory animals have been successful.

AGE.—Acute leukemias occur most frequently during the first five years of life and in the second decade. After the age of twenty-five its incidence is greatly diminished and its occurrence after the age of sixty is very rare. Chronic lymphatic leukemia has its chief incidence between the ages of forty and sixty; and the chronic myelogenous type occurs most frequently between the ages of twenty-five and forty-five and is excessively rare in infancy. All varieties may occur at any age, but the chronic forms are excessively rare after the age of seventy and the acute form after sixty. In children the diagnosis is often missed and the occurrence of leukemia in them is far more frequent than was supposed formerly.

SEX.—In all varieties there is a decided dominance of male incidence in the lymphatic forms, acute and chronic (nearly 2 to 1). In chronic myelogenous leukemia the disproportion is less marked but definite male predisposition is evident and especially marked in patients under twenty-five years of age and in those over forty-five.

HEREDITY.—No existing evidence justifies the assumption that any hereditary element is operative in leukemia.

Clinical Varieties.—One deals primarily with the two chief forms of leukemia, namely, (1) myeloid and (2) lymphatic, either of which may assume an acute form. These two diseases are readily separable clinically if existing in their usual chronic form, but with relation to both it must be remembered that in rare instances one encounters the disease in an acute stage or in a peculiarly puzzling transitional period.

Certain "mixed" cases of leukemia occur in which cells of both the granular and nongranular types appeared in the blood in excessive numbers, but it is now believed that the lymphocyte-like, nongranular cells are really premyelocytes originating like the granular leukocytes in the bone marrow. The same explanation applies to those cases in which a preëxisting typical picture of myelogenous leukemia becomes transformed to one of apparent lymphatic leukemia as the terminal stage is reached.

An acute myeloid leukemia may present the same blood-picture during life as an acute lymphatic leukemia though the actual disease may be readily demonstrable at autopsy, and indeed a critical examination of the white cells will show the dominant type to be myeloblastic or premyelocytic in type.

CHRONIC MYELOID LEUKEMIA

Symptomatology.—ONSET.—So insidious is the onset of chronic myeloid leukemia that cases are seen almost invariably only when well established and far advanced. The recognition of the disease early is usually wholly an accidental occurrence.

The early symptoms are those of a gradually developing anemia and one encounters chiefly fatigability, subjective sense of weakness, and perhaps some breathlessness upon exertion.

In certain instances the patient notices a swelling on the left side which is caused by the greatly enlarged spleen and quite commonly there is a complaint of a weight or a dragging sensation on the left side with or without pain due to perisplenitis.

The degree to which this disease may advance without causing symptoms severe and troublesome enough to bring the patient to a physician is astonishing, but the same statement may be made with relation to pernicious anemia, whether of the plastic or aplastic type. The author has in the rarest instances only encountered cases of myeloid leukemia in which there was not massive splenic enlargement and a typical blood-picture.

OUTWARD APPEARANCE OF PATIENT.—The outward appearance of the victim of leukemia may be that of perfect health and, just as one finds "rosy chlorotics," so he may encounter "rosy leukemics." Such instances are peculiarly frequent in individuals having a delicate skin and the heightened color usually reflects a secondary weakness of the circulation and instability of the vasomotor system.

In several cases of this kind seen by the author the outward appearance of the patient dressed for the street has been wholly normal unless one examined carefully the conjunctivæ or the pharyngeal mucous membranes, in which regions the anemia was manifested clearly, yet in several of these the splenomegaly was so pronounced as to bring the right edge almost to the anterior superior spine of the right ilium and the blood-picture was that of established, advanced and wholly incurable leukemia.

Usually, however, the victim of myeloid leukemia is pale and sallow or the skin may show a grayish pallor. Marked weight loss is common and many of these patients present typically a combination of emaciation, slender extremities and the "poached-egg" belly, the latter being due to the great enlargement of the liver and spleen together in many instances with the presence of an ascitic accumulation.

HEMORRHAGE.—In some instances attention is first directed to the serious condition of the patient by the occurrence of a severe and relatively intractable hemorrhage. In few diseases is the tendency to hemorrhage more pronounced and the results more serious. In every instance family members or friends who are about the patient should be warned of the danger of its occurrence and of the simpler means for checking it.

The loss of blood in such cases may occur from any mucous membrane with or without obvious and direct irritation or injury. The amount lost may be very large and in terminal cases may result directly in death, though, as a rule, the hemorrhage ceases or is controlled only to be repeated again and again until the patient dies from this added cause of exhaustion and inanition.

LUNGS.—Cough is a common symptom in many cases in which the disease is well established and this may be due to chronic bronchitis, or in the later stages to pulmonary congestion or actual edema. Pleurisy with or without effusion, or actual pneumonia are present in some cases.

Cardiovascular System.—The myocardial weakness in these cases, as they approach the terminal stage, may be profound. Effort dyspnea may be excessively troublesome and even walking on the level with the utmost slowness may produce it. The dyspnea and the myocardial weakness are intensified by the abdominal distention late in the disease. Gravity edema is present almost invariably in the later stages and general edema with a special tendency to serous accumulations, oftentimes abrupt in onset, in the peritoneal, pleural and other serous cavities may occur.

Hypertrophy is not present to any considerable degree in these hearts but dilatation, usually moderate, is not uncommon and it is manifestly impossible for any heart to maintain proper tonicity in the face of the blood condition present in this disease.

Glands.—Only in rare instances and in the terminal stages is there any decided glandular involvement and the massive enlargement of abdominal and mediastinal glands reported occasionally must be an exceedingly rare occurrence.

Purpura.—Most decided purpuric manifestations may be present especially in the later stages of the disease and with these in some instances there is an associated tendency to sudden large hemorrhages into the peritoneal or pleural cavities.

Leukemic Retinitis.—True optic neuritis, or markedly impaired vision, is seldom encountered but changes due to extravasation of blood or to leukocytic accumulations forming small growths is a comparatively frequent complication. Commonly the ophthalmoscopic findings are small, irregular, red-bordered whitish flecks lying along the vessels at the periphery of the fundus.

Deafness.—Cases of deafness are not uncommon and are probably due to hemorrhages. In some instances they assume the form of Ménière's syndrome; indeed hemorrhage into the labyrinth has been reported in a number of instances.

Genito-urinary Tract.—Aside from the fact that uric acid is present in excess and that the usual signs of chronic renal congestion may be present in terminal cases with marked myocardial weakness, there is little of importance to be observed clinically. A trace of albumin and an occasional hyalin and granular cast are common findings and in such instances the amount of urine is likely to be diminished.

Priapism has been reported as a comparatively frequent symptom, but oddly enough in a large series of cases coming under the observation of the author there has been no instance of it and the prevailing opinion at this time is that it is a very unusual symptom.

Metabolism.—Metabolism is increased greatly and patients frequently show a marked preference for room temperatures too low for the comfort of their attendants or family members.

Fever.—This symptom is present in about 70 per cent. of all advanced cases, the temperature tending to range from 101.5° to 103° F. (38° to 39.45° C.) and to show periods of remission or actual intermission. It constitutes one of the signs of the advanced stage of the disease and one of the factors of the comparatively rapid exhaustion which occurs at that time.

The Nervous System.—Aside from the occasional occurrence of cerebral hemorrhage as a terminal event, the nervous symptoms in leukemia are merely those of the anemia and are neither of great importance nor especially prominent in the course of the disease. Deafness and fundus changes have been referred to in a preceding paragraph.

GASTRO-INTESTINAL SYMPTOMS.—In some instances these are quite as troublesome as in pernicious anemia and, aside from anorexia, flatulence, and the like, may take the form of recurring attacks of diarrhea or dysentery most exhausting to the patient and occasionally accompanied by serious hemorrhages. In such cases the more serious symptoms are ascribable to leukemic infiltration of the walls of the stomach and intestine. These disturbances apparently have been more common in the series of cases observed by the author than in the case of many other observers who make little of the gastro-intestinal accidents of this disease. Hemorrhage from the bowels is an especially troublesome and exhausting symptom when it occurs.

THE LONG BONES.—Pain and tenderness over the long bones are symptoms encountered very frequently and in some instances the former may be a relatively early and distressing manifestation.

THE SPLEEN.—As has been stated previously, the spleen is usually markedly enlarged before the case presents itself to the physician and the tumor should present few difficulties with respect to diagnosis. The entire course of the development of the splenomegaly may be painless but not infrequently there is a history of more or less distress in the left upper abdominal quadrant or referred to the back. Any degree of enlargement may be encountered and in any event the edge is likely to be peculiarly well-defined because of the early change in the consistence of the organ.

In most instances observed by the author it has been quite easy to palpate the characteristic notches in the border and such mistakes as have been observed have arisen from the examiner's poor technic rather than from any obscurity in the physical signs. The tumor is directly movable in inspiration, receding promptly in expiration, is firm in consistence, carries a well-defined edge usually interrupted by the characteristic splenic notches referred to above, and may be followed by palpation and percussion back to the classical location of the spleen under the ninth, tenth, and eleventh ribs.

If the enlargement of the organ is marked, one may detect a friction sound or grating over it upon auscultation. Its size varies greatly from week to week, day to day, and even from hour to hour, and a failure to recognize this fact has been responsible for certain false conclusions as to the efficacy of certain lines of treatment.

Most of the errors encountered by the author in connection with the misinterpretation of the splenic tumors have been due apparently to the excessive size and the failure to recognize the great importance of direct movement in respiration as a sign and the need of following back from the free edge of any growth of this kind to the point of attachment in order that its original site and point of attachment may be ascertained.

THE LIVER.—The liver is demonstrable and usually a decided enlargement of it is readily detected in these cases. The edge is firm and smooth, making palpation easy and often revealing itself to inspection.

ASCITES.—In the author's experience ascitic accumulations have been common in the advanced stages of the ailment. No doubt leukemic infiltration is responsible in large degree for such fluid accumulation.

THE BLOOD-PICTURE.—The red cell-count is markedly reduced and the leukocytes are greatly increased in number, the average total count being

400,000 per cubic millimeter of blood in well-established and advanced cases, whereas the maximum may exceed 1,000,000 cells per cubic millimeter. It should be remembered that it is not the total number of white cells present which receives consideration, but the presence and numbers of such cells of marrow derivation. Nevertheless the total number of white cells present is of importance as indicating the severity of the case. The characteristically important cell in this disease is the neutrophilic myelocyte, occurring as it does in such numbers as to constitute 20, or in certain instances 40 or even 50 per cent. of the total leukocytes present. Eosinophilic and basophilic myelocytes also occur. Forms intermediate between the polymorphonuclears and the myelocytes (metamyelocytes) are often present.

The majority of leukocytes are polymorphonuclear neutrophilic cells which usually are increased both relatively and absolutely but even of these many show abnormalities in their size or in their nuclei. The percentage of these varies from 25 to 75 or 80 per cent., but there is also an absolute increase. The lymphocytes are increased, but their percentage is likely to be relatively low. The eosinophils are so increased as to maintain in many instances, or perhaps exceed, their normal ratio and, almost invariably, an absolute increase. Basophil granules may occur in either eosinophilic or neutrophilic polymorphonuclear cells.

Normoblasts are very numerous; megaloblasts, less so but sufficiently plentiful, and the mast cells are more numerous in myeloid leukemia than in any other disease. Polymorphonuclear basophils (mast cells) are markedly increased both absolutely and relatively. Myeloblasts are important but scanty elements in the blood-picture and care is necessary to distinguish them from the lymphocytes. The microblast is also a commonly observed form, adding to the bizarre appearance of the blood-picture.

STRIKING BLOOD-PICTURE.—One has only to refer to an actual mount of blood from a leukemic patient or to the textbook plate to see how absolutely striking and characteristic the appearance is and how little likely the physician is to be led astray. In most of the cases encountered by the author the erythrocyte count has run between 2,500,000 and 3,000,000 per cubic millimeter dropping as the disease advanced to 2,000,000 or even less per cubic millimeter.

Moderate grades of anisocytosis occur and usually a definite but not extreme poikilocytosis. Variations in the avidity of the cell for the stain are marked in all severe cases. In cases encountered fortuitously in the early stages there may be no demonstrable anemia and the myelocytes may be found with difficulty and only in small numbers. The color index in this disease is usually low; that is, the hemoglobin content of the individual cell is diminished as in chlorosis but this change is gradual and for a considerable period the hemoglobin value of the erythrocyte may be normal. The blood-platelets are increased sometimes very greatly.

ATYPICAL CASES OF CHRONIC MYELOID LEUKEMIA.—It must be remembered, first, that under treatment with the x-ray or large doses of arsenic, benzol and the like, or after the onset of some intercurrent acute infection, even though this be of short duration, the total white count may be nearly or quite normal; second, that under these conditions the white cells present may be dominatingly myeloblastic; and third, that the usual increased percentage in the polymorphonuclear basophil and eosinophil cells may be lacking.

Diagnosis of Chronic Myeloid Leukemia.—From the foregoing discussion it is obvious that the diagnosis of chronic myeloid leukemia should be perfectly simple in nearly every instance for any one of adequate training and possessed of proper laboratory facilities. The blood-picture usually is striking and absolutely clear in its meaning. The enlargement of the spleen in association with the blood-picture makes a diagnostic combination present in no other ailment.

Complications and Sequelæ.—Aside from hemorrhage and the symptoms indicative of myocardial insufficiency there are few complications in any way peculiar to or unusually associated with chronic myeloid leukemia. Tuberculosis may become active and pursue an acute miliary or chronic progressive course, and any one of the acute infections may be superimposed accidentally upon a leukemia. It should be remembered that the onset of any acute infection such as pneumonia, typhoid, influenza, or one of the acute exanthemata may produce a very marked temporary amelioration in the leukemic manifestations. This change may be so marked as to bring the blood findings almost to normal, but is of short duration and in some instances such a remission is followed by a change in the type of the disease, which, formerly chronic and sluggish in its progress, may become acute and progressively fatal.

Pathology.—BONE MARROW.—The bone marrow in this disease appears at autopsy in most instances pale pinkish or yellowish gray and relatively firm in texture. In rarer instances it carries a greenish tint. The tissues are crowded with cells of all varieties known to this region, both leukocytic and erythrocytic, although the dominant feature of the intense hyperplasia is the myeloid cell.

THE HEART.—There are no changes in the heart characteristic in themselves of chronic myeloid leukemia, but degenerative changes are extremely common and fatty degeneration is very often present and occasionally extreme. Within the heart one finds often at autopsy yellowish white growths which, because of the great number of contained leukocytes, suggest a mixture of pus with the fibrin. Microscopical examination may reveal leukocytic infiltration and in certain unusual instances thrombosis of the coronary branches may cause areas of softening (myomalacia cordis).

THE SPLEEN.—The spleen usually is enormously enlarged, its weight varying from 2 to 18 or 20 pounds. The normal splenic outline is in great measure preserved, including its notches usually easily palpable in this disease whatever the degree of splenic enlargement. Its consistence is firm, its surface smooth, and the normal color is usually changed to a grayish tint. Under the knife it cuts with difficulty because of the great increase of fibrinous tissue in its stroma. Hemorrhagic infarctions are not uncommon and the splenic tissue is found to contain an enormous number of cells which consist chiefly of myelocytic forms with either eosinophil or neutrophil granules.

LIVER.—This organ is markedly enlarged in most instances and its capillaries contain large groups of myeloid cells similar to those found in the spleen and bone marrow.

CHRONIC LYMPHATIC LEUKEMIA

Definition.—Chronic lymphatic leukemia is characterized not only by an increase in the total leukocytes present in a given blood but particularly by the enormous preponderance of lymphocytes (90 per cent. or more) and the wide-spread enlargement of the lymphatic glands.

Etiology.—As in the case of the chronic myeloid type of leukemia, the etiology of the lymphatic form is still wrapt in mystery. Certainly there has been no single basic cause proven and although the suggestion of a specific infection is strong and has been supported apparently at times in recent years by announcements of supposed causative microörganisms recovered from the blood and tissues of patients, nothing has been proven definitely. A vast number of hypotheses have been formulated, particularly by German and Austrian investigators, but for the most part these have proved to be baseless assumptions or the result of faulty experimentation.

AGE AND SEX.—The age incidence is largely between the forty-fifth and sixtieth years and it is seen but rarely at the extremes of life. With regard to sex, male preponderance is very decided, varying at different age periods from 75 to 80+ per cent.

Symptomatology.—CLINICAL HISTORY.—The onset of a lymphatic leukemia of the chronic type is usually gradual and insidious, few cases being recognized during the earlier stages. As a rule there has been an antecedent enlargement of the lymphatic glands or a swelling of the tonsils may have been noticed. The tumors present are as a rule separated and movable, free from active inflammatory change, and showing little or no tendency to suppuration. These seldom exceed an egg in size and as a rule do not reach such large proportions.

In most instances all accessible glands are found to be affected in some degree or become so during the course of the illness. In certain of the acute cases particularly, the enlargement of the superficial glands may not be excessive though those of the internal groups may take on rapid and extreme enlargement and produce symptoms of a grave and even fatal character.

The glands of the cervical chains are most prominent ordinarily but marked enlargement may be present in the axillary or inguinal groups and, furthermore, nodes ordinarily inconspicuous may form large tumors. In most instances the enlarged glands are painless and free from tenderness.

KIDNEYS.—The urine usually contains albumin and casts.

SPLEEN.—The spleen is moderately or decidedly enlarged, but so far as the outward symptoms go the glandular changes dominate the clinical picture. It is usually readily palpated but ordinarily does not descend more than one or two fingers' breadth below the costal margin.

FEVER.—Fever is present in variable degree in all acute cases and in the later stages of the chronic form. Disturbances of vision are of unusual occurrence, but "leukemic retinitis" or retinal hemorrhages may occur.

TONSILS.—Enlargement of the tonsils may be a relatively early symptom and lead to unfortunate results through incautious operative procedure.

PRESSURE SYMPTOMS.—In advanced cases or in acute cases with rapid and extreme enlargement of the internal glandular groups the symptoms of pressure may be extreme and, especially in such cases as show marked mediastinal growths, a horrible picture of death by chronic slowly progressive suffocation is presented.

HEART AND LUNGS.—No specific changes occur but as in myelogenous leukemia a profound myocardial decompensation may be induced and pleurisy and pericarditis occur.

Gastro-intestinal Symptoms.—These may be marked, moderate, or in large part absent and take the form usual in such anemias, namely, flatulence, epigastric oppression, anorexia, nausea, or perhaps vomiting or diarrhea. In addition there may be serious hemorrhage from the stomach or bowel or from both.

Skin Lesions.—These may be very troublesome symptoms in this form of leukemia and any one or more of a large group may be present during the course of the disease. Urticaria, pruritis and prurigo may prove especially troublesome but in addition to these vesicular, pustular, petechial, and nodular lesions as well as infiltrations, hematomas and actual tumor formations may occur. Lesions show on section typical leukemic lymphocytic infiltration.

Nervous System.—Only in the rarest instances do specific lymphomatous deposits or growths occur in the spinal cord or brain.

Subjective Symptoms.—Unless enlargement of the glands is marked and noted by the patient he is unlikely to present himself to the physician until subjective weakness and fatigability force him to do so. This seldom occurs until the blood changes are marked and in most instances glandular enlargement is easily detected.

Outward Appearance.—These patients ordinarily show a simple pallor though they are occasionally sallow or gray. In such as have mediastinal pressure symptoms or abdominal growths, a peculiarly harassed drawn physiognomy may be encountered.

The Liver.—The liver is usually firm in consistency and moderately enlarged, but in some instances the organ is tremendous in size.

Blood Findings.—It must be remembered that the essential feature of the blood-picture in lymphatic leukemia is the presence of an absolute monocytosis, the mononuclear cells constituting from 90 to 99 per cent. of the entire leukocytes present. Obviously, any blood examination in one of these cases will show that the mononuclear leukocytes will dominate the microscopic field.

The total blood-picture lacks the diversity of form and type in the white and red cells alike, so characteristic of myeloid leukemia. Nucleated red cells are not plentiful, though in the acute type of the disease and in certain of the leukemias of childhood they may be present in considerable numbers. If present, the normoblast is the predominant type of nucleated red cells. There is a considerable amount of cell deformity and polychromasia. Anisocytosis is marked and basophilic stippling may be noted.

The total leukocyte increase, while definite and striking (the average lying between 200,000 and 250,000 per cubic millimeter of blood), is seldom as marked as in leukemia of the myeloid type and may be less than half these figures. The maximum leukocyte count in these cases is placed at 1,000,000 cells per cubic millimeter, but in a case encountered by the author the figures reached 2,133,000 for the single examination possible. This probably represented a preagonal increase as the count was made only twenty-four hours before death occurred.

While apparently identical with the normal lymphocyte, these cells will in large part show certain differences in their staining. Faint staining of nuclei and protoplasm, entire lack of "azure granules," marked variation in size, and evidence of fragility may be noted, the last through the presence of aggregations of protoplasm in the smear.

Diagnosis.—As in the case of chronic myeloid leukemia, so in the chronic lymphatic form, there is really but slight excuse for an error in diagnosis, provided only that the examining physician shall neither be grossly careless nor lacking in the necessary equipment for the examination of the blood and the ability to use it.

The combination of the outward symptoms of anemia, progressive weakness and fatigability, enlargement of accessible lymphatic glands, and a blood-picture showing clearly a large increase in the number of leukocytes present and an absolute dominance of the mononuclear cell in the leukocytic field leaves no excuse for errors save in the rarest instances.

It is important to remember that the chronic cases may have endured for long periods without recognition, inasmuch as the disease may be only very slowly progressive and the glandular enlargements may have been present for years without attracting the attention of the patient, or at all events creating in him any alarm. So far as the glandular masses themselves are concerned these seldom or never assume the large dimensions seen in Hodgkin's disease and, furthermore, in the latter ailment the blood changes characteristic of lymphatic leukemia are lacking.

THE ANEMIA.—It should be borne in mind that a variable degree of anemia may be present in these cases and that in some instances this may be so extreme as to be somewhat misleading. In the larger number of cases the red blood-count will be found to run below 3,000,000 cells per cubic millimeter and in about one-third of the cases encountered below 2,000,000. As the disease advances the count falls, showing remissions however, as in pernicious anemia, and finally dropping definitely below 2,000,000 as the end approaches. The color index is usually low until the erythrocytes are clearly reduced in the later stages of the disease, when the hemoglobin content of the individual cell may be high, yielding a high color index.

In other words, in cases of chronic lymphatic leukemia showing a red blood-count running from 3,000,000 to 4,000,000 cells per cubic millimeter one would expect to find a low color index, whereas in cases approaching or entered upon the terminal stage with counts below 2,000,000 cells one would find the high color index. In certain instances a diagnosis of pernicious anemia has been wrongly made.

Complications and Sequelæ.—The chief complications of chronic lymphatic leukemia relate to the effects of pressure and the occurrence of hemorrhage; otherwise there are no conditions which are worthy of specific consideration.

Treatment of Chronic Leukemias.—In the rare instances in which one encounters chronic leukemia, whether myeloid or lymphatic, in its earlier stages it is perfectly justifiable to use any and all methods of treatment which have proved useful in securing remissions in the established or advanced cases but in these latter groups long periods of relative quiescence occur and it may be unwise to use, during these periods of peculiar calm and lack of progression, the more radical forms of treatment such as the x-ray. A reason for this is found in the peculiar liability to violent relapses and not infrequently to the terminal crises in the case of patients so treated, these occurring at times when the maximum improvement is manifest.

TWO CHIEF THERAPEUTIC METHODS.—**Roentgen radiation** and the administration of benzol are the two therapeutic agents most productive of striking results. In the case of both, results are most striking in the myeloid form. Roentgen radiation would seem to modify the excessive activity of the leukopoietic tissues and aid in destroying the excess of leukocytes in the circulation.

PRECAUTIONS TO BE OBSERVED.—There are certain dangers inherent in the use of x-ray radiation which must be always kept in mind. The liability to burns and the evil effect of these, especially when produced in an undernourished and devitalized patient, is well understood, and these are avoided by setting apart specific and definitely outlined areas over the spleen, superficial lymphatic glands and the long bones and using different portions of these areas from time to time to avoid repeated recurrent exposure of the same area so far as possible.

Radiations of five, ten, or twenty minutes' duration are used and the period is varied according to the judgment of the skilled operator who alone should attempt to use such therapeutic methods. In every instance the earlier exposures should be relatively widely separated and of short duration and the idiosyncrasies of the individual patient should be considered and guarded against. Overtreatment and undertreatment alike may intensify the very process which it is intended to moderate or suspend.

If the toxic symptoms are severe and the temperature high, and the glands undergoing enlargement despite treatment, it is usually unwise to push it. There can be no doubt that under x-ray treatment a large number of apparent arrests have occurred, some of considerable duration, but in the long run it proves that the fatal issue has merely been postponed.

BENZOL.—Benzol is a powerful leukocytic poison, powerful for good or for evil according to the method and manner of its use and the response registered by the individual patient. On the whole it would appear to be a better agent for therapeutic use in the leukemias than the x-ray, radium, or large doses of arsenic. In favorable cases the administration of this drug is succeeded by a slight increase in the number of leukocytes present in a given blood and later a striking diminution chiefly affecting the polymorphonuclear cells.

If favorable effects continue the pathologic types of white cells tend to disappear and a normal differential leukocyte count may be found attainable. The drug is much more valuable apparently in the myeloid form of leukemia than in cases of the lymphatic type. Improvement of the blood condition is attended usually by a more or less parallel favorable change in the spleen, liver and lymphatic glands. Excessive use of the drug may produce an aleukemia or an aleukemic state associated with a severe form of anemia.

Disturbances Attending the Use of Benzol.—Headache, vertigo, bladder irritability, impotence, gastric disturbances, and evidence of renal congestion may occur and demand immediate cessation of administration.

Method of Administering Benzol.—Benzol may be administered in capsules with olive oil. The initial daily dose is 30 grains (1.95 grams) and the maximum of 75 grains (4.87 grams) daily is reached during the course of one week. The maximum daily dose of 75 grains may be continued until the leukocyte count is 30,000 per cubic millimeter of blood or under, but one should watch carefully for toxic symptoms.

Thorium X may be used advantageously in many instances to supplement the action of the x-ray. This substance has the advantage of being relatively harmless though not wholly so, and of permitting more exact dosage than is possible with other methods.

THE USE OF ARSENIC.—**Arsenic** was formerly the drug of preference for use in this disease and under its administration in some instances apparent or actual arrest or remission occurred. On the other hand a great many accidents due to poisoning arose and at present one would by preference seek to use or have used the other agencies herein described.

The preparation of arsenic best adapted to therapeutic purposes for use in this disease is **Fowler's solution (liquor potassii arsenitis)** and the initial daily dose of 30 minims (1.90 c.c.) should be raised each day one drop over the dose of the day preceding until a daily dosage of 200 minims (12.32 c.c.) is reached. It may then be continued on that level with due precautions against chronic arsenical poisoning.

The associated high grade of anemia so generally encountered in established cases of leukemia is dependent no doubt upon a general and extreme impairment of nutrition, the disturbance in the hemopoietic organs throughout the body, and the presence in the circulation of powerful toxins which tend to promote hemolytic changes. The form which this associated anemia takes distinctly calls for the administration of **iron** which may be administered in exactly the same way and through the same agency and preparations as one would use in chlorosis. The author has had no experience with the treatment of leukemia by intramuscular injections of defibrinated blood and such reports of this treatment as are accessible are not such as to make advisable its continued employment.

TUBERCULIN INJECTIONS AND THE USE OF BACTERIAL TOXINS.—The administration of **alien leukemia serum**, of **splenic extracts**, of **formalin**, and of **cinnamic acid**, has been recommended by various investigators but the methods have attained no prominent place in the therapy of leukemia.

SPLENECTOMY.—Of this procedure one need say only that it is contra-indicated absolutely. The gastro-intestinal disturbances so common in this ailment are treated exactly as would be the case if they existed apart from it. The same can be said of cardiovascular upsets and of actual edema or dropsy.

CONTROL OF HEMORRHAGE.—One of the most essential matters in connection with the treatment of hemorrhage is the warning to be given to the patient and the members of the famliy who are around him and associated with him. As stated previously, it is an easy matter to place in the hands of family members or of the patient himself certain of the simpler remedies together with a description of the means by which spontaneous hemorrhage may be controlled. Some of the ghastliest pictures the author has ever witnessed have been those which represented the unexpected occurrence of profuse, persistent hemorrhage in people remote from medical care and especially distant from skilled specialists whose care in severe cases was distinctly indicated. A description of the methods commonly employed for controlling hemorrhages of this kind will be found under "Hemophilia."

GENERAL MEASURES OF TREATMENT.—It will be understood that to a large extent leukemic patients will require treatment of a symptomatic sort and varying from time to time with the particular conditions present in a given case. Furthermore, fresh air, sunshine, proper feeding, and pleasant environment are as essential here as in any other ailment.

Importance of Rest.—The author has been impressed particularly by the common failure to insist upon a proper degree of physical rest for the leukemic, and, in general, profoundly anemic patients. Everything representing overexertion operates directly against the good effects of any specific therapy attempted and oftentimes no real advantage can be gained until this important factor is recognized and met. What constitutes overexertion varies with the individual case and from day to day and week to week oftentimes in the patient under observation. Again and again individual cases which have proven previously almost wholly refractory under treatment have improved immediately following the institution of rules adequate to secure a maximum of rest.

Special Importance of Feeding.—Without laying down any rules or elaborating any fixed dietary, the author would emphasize the value of adequate and appropriate daily intake of food for these cases. Gastrointestinal disturbances are frequent and patients in large measure represent individual problems for the dietitian. So far as possible monotony should be avoided and the taste of the patient, which is often capricious, may be followed with benefit in many instances and even in relation to articles of food which may seem improper under the existing conditions. As was said with reference to rest, so one may say with regard to proper nutriment, that unless it be properly attended to, the good effects of any specific treatment may be held in abeyance or fall far short of the maximum effectiveness obtainable.

Prognosis.—The chronic forms of leukemia endure for periods varying from four months to five or six years. The late Sir William Osler has stated that in his experience the chronic lymphatic form seems to be the most protracted. In the experience of the author the myeloid form on the whole has shown the longest duration. The acute cases result in death within three months and the chronic cases do not recover although remissions, intermissions and even apparent arrests are common and may continue over considerable periods of time.

Pathology.—GLANDS.—As might be expected from the clinical appearances in this disease, the dominant factor in the postmortem appearances in chronic lymphatic leukemia is the glandular enlargement which is practically universal and of a degree readily recognizable. The glands vary in size greatly but seldom exceed that of a large English walnut. As might be anticipated, the outline of the gland is usually maintained and there is seldom any tendency to fusion manifest.

On section the gland appears soft and gray or pinkish gray in color, smooth, and homogeneous. The tissue is packed with lymphocytes which are dominantly of the small type and not only fill the vascular spaces but infiltrate the surrounding tissues.

SPLEEN.—The spleen almost invariably shows decided enlargement in chronic lymphatic leukemia but does not reach the enormous dimensions so characteristic of the chronic myeloid form of this disease. Its consistence is variable, the acquisition of any decided firmness in texture depending apparently upon the longer or shorter duration of the disease. Infarcts are met with frequently but the surface of the spleen itself is smooth and the normal outline preserved. The substance of the organ is filled with infiltrating lymphoid cells and the microscopic structure is thereby rendered almost unrecognizable.

Bone Marrow.—As in the case of chronic myeloid leukemia the bone marrow is gray or grayish red in color, dense, and usually homogeneous. Microscopically it shows almost complete replacement of the normal erythroblastic and myeloblastic tissue by lymphoid cells.

Liver.—The liver is usually definitely and often greatly enlarged, the only characteristic feature being the collections of lymphocytes forming perivascular nodules in the connective tissue. Leukemic deposits may be found in various tissues of the body including the meninges, integument, trachea, larynx, the nerves themselves and the kidneys. The tonsils are usually enlarged as might be expected from the clinical history of the case and its lymphocytic infiltration throughout the intestinal tract.

ACUTE MYELOID LEUKEMIA

The appearance of myeloid leukemia as an acute ailment is excessively rare, but, as has been stated previously, it may and does occasionally occur and may go on to a sufficiently full development of the blood-picture to permit differentiation or may prove fatal while the patient is still presenting a blood-picture indistinguishable by the general practitioner from that of acute lymphatic leukemia because of the difficulty in differentiating the lymphoblast from the myeloblast.

Course of Acute Myeloid Leukemia.—The course of this ailment is that of an extremely grave and acute infectious disease showing a pronounced hemorrhagic tendency, rapidly developing extreme anemia and high fever. It will be noted that the distinction between acute and chronic leukemia is more definitely indicated in the mode of onset than by the duration of the disease, which, in acute cases, does not exceed four months and may be much less. The onset of such an acute form is abrupt, stormy, and in every way characterizing a severe infection.

Etiology.—The etiologic factor in these acute forms is not known though the suggestion of a basic infection is, of course, obvious. Indeed, for the greater part, the attacks follow some suppurative or distinctly infectious ailment such as furuncle, tonsillitis, dental abscess, etc.

Age.—With respect to age, it may be said that at no age is there complete immunity but that children and young adults are oftenest affected whereas elderly individuals and infants almost wholly escape.

Symptomatology.—One of the most suggestive associated symptoms, at once indicating a blood examination if none has been made previously, is hemorrhage from the mucous membranes, which may be preceded by hypersensitivity of the buccal and pharyngeal surfaces. The combination of fever accompanied by a rapidly-produced and striking anemia is in itself suggestive, and some enlargement of the cervical glands is present save in the rarest instances of this disease.

It is obvious that the inflamed mucous membranes may yield striking symptoms of an actual pharyngitis, stomatitis, or both conditions combined. In these cases the mucous membranes may be greatly swollen and the bleeding may occur at the slightest touch or without any known injury.

The associated glandular chains enlarge rapidly and become excessively swollen and tender in nearly all cases. In some instances, moreover, the tonsils play a dominant and somewhat misleading part and, together with the gums, may undergo necrosis or actual gangrene. Reported cases with a well-attested diagnosis are rare, but it is probable that many are overlooked.

Clinical Types.—The disease may be mild and in extremely rare instances associated with glandular involvement of only a mild type and no hemorrhagic tendency. In such cases an acute infection associated with a high grade of anemia with fever will be the suggestive combination.

In other cases the hemorrhagic features obscure everything else and may lead to a diagnosis of purpura hemorrhagica. In yet others the ulcerative or gangrenous process in the buccal and pharyngeal mucous membranes may dominate the clinical picture and no striking tendency to hemorrhage exist. The exhaustion is profound, the pulse is rapid and labile, hæmic murmurs are present, and precordial oppression may be present. It should be remembered that either pleuritis or pericarditis may be present with or without effusion.

The spleen is palpable usually, but rarely enlarged to any great degree. The urine usually contains a trace of albumin and an occasional cast. The liver is demonstrable though but slightly enlarged in most instances and gastro-intestinal disturbances are in some cases very severe, and diarrhea or vomiting may be associated with hemorrhages.

BLOOD-PICTURE.—If the blood is examined shortly after the onset the appearance may be most misleading in that the count is usually subleukemic or actually aleukemic in very rare instances. The number of white cells usually does not exceed 25,000 or 30,000 per cubic millimeter and may not exceed a few thousand.

The important cells from the standpoint of early diagnosis are the bone-marrow derived myeloblasts or rather the premyelocytes which represent a transition stage between the myeloblast and the myelocyte and resemble closely the large lymphocyte for which they are mistaken ordinarily.

Their recognition depends upon the demonstration of fine neutrophilic granules in the cell protoplasm or their reaction to the indophenol-blue or guaiac tests which serve to demonstrate the presence of phenolase and peroxidase, substances which are absent in the lymphocytes.

The white blood-count tends to rise somewhat rapidly and may in the course of a few weeks reach several hundreds of thousands but the extreme high counts are rare. A deceptive picture of pernicious anemia may be presented in certain very acute and malignant cases, if the leukocyte increase is slight or lacking, so far as the red cells are concerned. Anisocytosis and polychromatophilia may be very marked and normoblasts and megaloblasts plentiful.

COURSE OF THE DISEASE.—The course in this ailment is stormy and resistless in most instances.

Treatment.—The treatment of acute myeloid leukemia is wholly symptomatic.

Prognosis.—As stated, the course of this disease usually is stormily progressive and resistless, but in rare instances transient remissions occur and a few cases of recovery have been reported, but such reports must be received with caution.

Pathology.—The autopsy findings show classical proliferations of myeloid leukopoietic tissue both in the marrow and extramedullary and accessory sites such as the liver, spleen and lymph glands. In all true cases these changes are so great as to amount to a definite transformation but histologic study is required to determine whether or not the proliferation is one affecting the cells of bone-marrow derivation type and not the lymphocytes.

The bone marrow itself should show a dominance and excessive number of myeloblasts, myelocytes and premyelocytes and the spleen, liver and lymphatic glands also should show the dominance of such cells.

The postmortem findings in acute myeloid leukemia vary only slightly from the chronic form save that the changes such as would require greater time duration are more prominent in the latter than in the former ailment.

ACUTE LYMPHATIC LEUKEMIA

Definition.—This is a progressive and fatal disease of unknown causation characterized by a relatively sudden or acute onset, fever, marked prostration, and a tendency to necrotic or gangrenous processes in the mucous membranes of the mouth and throat, hemorrhages from mucous membranes, with no constant or invariable enlargement of the lymph glands, liver or spleen, and a blood-picture of severe and progressive anemia and a lymphocyte content varying from a moderate or great pathologic increase to a normal count.

Etiology.—The causes are wholly unknown. The incidence of the disease falls upon the earlier years of life.

Symptomatology.—The symptomatology is embraced by the definition as previously given. The onset of the disease is sudden, with or without a chill, and presents the symptoms of severe acute infection with profound prostration, aching, fever progressively increasing in height and in some instances nausea and vomiting. Patients may complain of sore mouth or difficulty in swallowing from the beginning, or these symptoms may become prominent later.

The picture is one of a severe infection attended by stomatitis, hemorrhages from the gums, and tonsillar swelling, followed by the development of a general tendency to hemorrhage. Unfortunately such cases lack marked glandular enlargement at the outset nor does it become a marked feature invariably later in the course of the disease.

The spleen and liver are seldom enlarged at the outset and the former may remain nonpalpable throughout, though a moderate enlargement is frequently present late in the disease. The urine contains an excess of uric acid, albumin and casts.

BLOOD-PICTURE.—Certain rare cases are aleukemic throughout and in a considerable proportion there is no marked lymphocytic increase at the onset. Usually however the distinctive pathologic increase is present a few days after the onset of the attack and the lymphocytes tend to increase progressively and at first quite rapidly. The count commonly attains figures varying from 30,000 to 80,000 but 100,000 to 200,000 lymphocytes per cubic millimeter may be present or the count may run up to double the latter figure.

Polymorphonuclear cells are present in small numbers but the lymphocytes not only dominate the blood-picture but ultimately constitute from 90 to 96 or 97 per cent. of the white cells present in many cases. In the very early stages or during certain phases of the disease it may run much lower in percentage, or, as stated, the case may be aleukemic so far as the blood-picture is concerned.

The erythrocytes drop rapidly from normal or slightly subnormal figures to those indicative or more or less profound anemia and in some cases nucleated red cells appear. The hemoglobin follows the same tendency to progressive diminution and in most instances keeps pace with it, yielding with respect to this phase of the blood-picture the relative equality of cells and coloring matter which one sees in ordinary chronic secondary anemia. In terminal stages, however, the hemoglobin value of the erythrocyte may fall greatly as in chlorosis. Thus, one finds either a normal or low "color index." The blood-platelets are diminished usually and any myelocytes that may appear are of no special diagnostic or prognostic significance.

Diagnosis.—This is suggested clearly in the discussion of the symptomatology and in most cases made easy by the blood-picture. The chief source of error is in a failure to appreciate the necessity for a study of the blood smear in cases of acute febrile onset with mouth and throat symptoms with or without a tendency to hemorrhage.

Treatment.—This is wholly symptomatic.

Prognosis.—The disease is probably fatal in all cases, the duration varying from a few weeks to three or four months. A few cases of apparent recovery are reported but are viewed as dubious from the diagnostic standpoint.

Pathology.—The postmortem findings in acute lymphatic leukemia vary only slightly from the chronic form save that the changes such as would require greater time duration are more prominent in the latter than in the former ailment.

BIBLIOGRAPHY

Leukemia

ACHARD, C., AND OTHERS. Comptes rend. de la Soc. de Biol., 1908, lxv, 56.

ADLER, E. Jahrb. f. Kinderh. u. phys. Erziehung, 1914, lxxx, 290.

AMBROZIO. Giorno Internal. d. Sc. Med., 1908, 18. Synop., Arch. Mal du Coeur, Mar., 1909.

ARNDT, C. Jour. A. M. A., 1914, lxiii, 1268.

ASKANAZY, S. Deutsch. Arch. f. klin. Med., 1900, lxviii, 34.

AUBERTIN, C. Semaine méd., Paris, 1905, xxv, 277.

AUBERTIN, C., ET BEAUGARD. Synop. in Arch. Mal. du Coeur, 1908, 655.

AUBERTIN, C., ET DELAMARRE. Soc. de Biol., March 14, 1908.

AUBERTIN, C., ET MOREL, T. Arch. d. mal. du Coeur, 1913, vi, 201.

AUER, J. Amer. Jour. Med. Sc., Philadelphia, 1906, cxxxi, 1002.

AUSTRIAN, C. R. Johns Hopkins Hosp. Bull., 1911, xxii, 298.

BARKER, L. F. Diagnosis of internal disease. In Monographic Medicine, Vol. III, p. 208, D. Appleton & Co., New York, 1919.

BARKER, L. F., BAETJER, W. A., AND MILLER, S. J. Trans. Assoc. Amer. Phys., Philadelphia, 1915.

BARKER, L. F., AND GIBBES, J. H. Johns Hopkins Hosp. Bull., 1913, xxiv, 363.

BARRENSCHEEN, H. K. Wien. klin. Wchnschr., 1912, xxv, 293.

BECLERE ET BECLERE. Cog. Intern. de Physiothér., Paris, 1910. Soc. de Radiol. Méd. de Paris, April, 1909; synop. in Arch. Mal du Coeur, Nov., 1909; synop. Folia Hæmat., July, 1910. Strahlentherapie, Berlin, 1913, iii, 553. Trans. Internat. Cong. Med., London, 1914.

BELTZ, L. Deutsch. Arch. f. klin. Med., 1913, cxiii, 116.

BENNETT, J. H. Edin. Med. and Surg. Jour., 1845, lxiv, 413.

BERNHARDT, R. Arch. f. Dermat. u. Syph., 1914, cxx, 17.

BETTENCOURT, N. Comptes rendus de la Soc. de. Biol., 1915, lxxvii, 188.

Beumelberg, K. Beitr. z. Klinik d. Tuberkulose, 1912, xxiii, 287.

Bickel, A. Moderne Radium- und Thoriumtherapie. Berlin, 1914, A. Hirschwald.

Billings, F. Jour. A. M. A., 1913, lx, 495.

Billings, F., and Capps, J. A. Amer. Jour. Med. Sc., Phila. and N. Y., 1903, cxxvi, 375.

Billings, F., and Rosenow, E. C. Jour. A. M. A., 1913, lxi, 2122.

Blumberg, F. Mitt. a. d. Grenz-geb. d. Med. u. d. Chir., 1912, xxiv, 516.

Boardman, W. W. Cal. State Jour. Med., 1915, xiii, 348.

Boechat, J. Frankfurter Zeit. f. Path., 1913, xiii, 489.

Boggs, T. R., and Guthrie, C. G. Johns Hopkins Hosp. Bull., Baltimore, 1913, xxiv, 368.

Bohland, K. Berl. klin. Wchnschr., 1893, xxx, 417.

Bottelli. Osp. Maggiore, Milano, 1920, 3. s., viii, 3-9.

Bovie, W. T. Radiations and their effects. Oxford Medicine, Vol. I.

Bradenburg, K. München. med. Wchnschr., 1900, xlii, 183.

Bunting, C. H., and Yates, J. L. Trans. Assn. Amer. Phys., 1916, xxxi, 165.

Yates, J. L. Johns Hop. Hosp. Bull., 1915, xxvi, 376.

Butler, J. Arch. Dermat. and Syph., Chicago, 1920, n. s., ii, 594.

Cabot, R. C. Osler and McCrae's "Modern Medicine," 1915, IV. A guide to the clinical examination of the blood for diagnostic purposes. Wm. Wood & Co., New York, 1904.

Cailliau, F. Bull. et mém. Soc. Anat. de Paris, 1920, xc, 506.

Capps, J. A., and Smith, J. B. Jour. Exper. Med., 1907, ix, 51.

Case, J. T. Surg., Gynecol. and Obs., Chicago, 1915, lxx.

Cassel. Berl. klin. Wchnschr., 1898, xxxv, 76.

Cawadias, A. et Monpherato. Comptes rend. de la Soc. de Biol., 1917, lxxx, 935.

Chalier, J., et Cremien, R. Progès méd., Paris, 1920, 3. s., xxxv, 57.

Cheney, W. F. Amer. Jour. Med. Sc., Phila. and N. Y., 1912, cxliii, 22.

Churchill, F. Amer. Jour. Med. Sc., 1904, cxxvii, 565.

Citron, J. Deutsch. med. Wchnschr., Leipzig u. Berlin, 1914, xl, 629.

Cohnheim. Med. klin., 1907, Hft. 41; synop. Fol. Hæmat., 1909, viii, 1. Virchow's Arch., 1865, xxxiii, 451.

Courmont, J., et Montagard, V. Comptes rend. de la Soc. de Biol., 1900, lii, 643.

Decastello, A. v. Zeit. f. klin. Med., 1909, lxvii, 319. Wien. Arch. f. inn. Med., 1920, i, 335.

Decastello, A. v., und Kienbock. Synop. Arch. Mal. du Coeur, 1908, 327.

De Luca. La cura della leucemia mediante i raggi x. Policlin., Roma., 1907, xiv, sez. med.; also Arch. d. farmacol. sper., Siena, 1907, vi, 18-25.

De Negri, A., und Mieremet, C. W. G. Centralbl. f. Bakt., Orig., 1913, lxviii, 292.

Desplats. Cong. Intern. de Physiother., Paris, 1910; synop. in Arch. Mal du Coeur, 1908, xx, 85. Jour. de Sc. Méd. d. Lille, May 22, 1909; synop. in Arch. Mal du Coeur, Jan., 1910, p. 62.

Dickson. Lancet, London, 1906.

Dietrich, A. Folia Hæmat., 1912, xlii, 43.

Dock, G. Philadelphia Med. Jour., 1900, v, 741.

Dohrer und Pappenheim, A. Folia Hæmat., Leipzig, 1913, xvi, 145.

Domarus, A. von. Folia Hæmat., Leipzig, 1908, vi, 337.

Dominici et Barcat. Arch. Mal du Coeur, 1908, 153.

Dominici. Comptes rend. de. la Soc. de Biol., 1900, lii, 851.

Donecke, F. Med. Klinik., Berlin, 1920, xvi, 781.

Dori, B. Wien. klin. Wchnschr., 1913, xxvi, 2034.

Drinker, C. Oxford Medicine, Vol. II, Chap. xv.

Dunn, J. S. Quart. Jour. Med., Oxford, 1913, vi, 293.

Dupeyral. Marseille Méd., April 15, 1909.

Eason, J. Lancet, London, 1918, cxciv, 637.

Ebstein, W. Deutsch. Arch. f. klin. Med., 1889, xliv, 343.

Ehrlich, P. Farbenanalytische Untersuchungen zur Histologie u. Klinik des Blutes. Berlin, A. Hirschwald, 1891.

Elischer und Engel. Zeits. f. klin. Med., 1909, lxvii, 31.

Ellermann, V. Zeits. f. klin. Med., Berlin, 1913, lxxix, 43.

Ellermann, V., and Bang, O. Centralbl. f. Bakteriol., 1 Abt., Jena, 1908, xlvi, Orig., 595.

Ellermann, V., and Bang, O. Hyg. u. Infektionskr., 1909, lxiii, 231.

Erb, W. H. Deutsch. med. Wchnschr., 1907, xxxiii, 833.

Fabbretti, A. Folia med., Napoli, 1920, vi, 395, 409, 445.

FALTA, W., KRISER, A., UND ZEHNER. Münch. med. Wchnschr., 1912, lix, 734.

FERRATA, A. Atti d. R. Accad. med. chir. di Napoli, 1919, lxxiii, 85.

FRAENKEL, A. Deutsch. med. Wchnschr., 1895, xxi, 639.

FRAENKEL, E. Virchow's Arch. f. path. Anat., 1914, ccxvi, 340. Münch. Med. Wchnschr., 1911, lvii, 1266.

FRAENKEL, E., UND MUCH, H. Münch. med. Wchnschr., 1910, lvii, 685.

FRIEDREICH, N. v. Virchow's Arch., 1857, xii, 37.

FUCHTNER, E. Med. Kor.-Bl. f. Wurttemb.-Stuttg., 1920, xc, 113.

GASBARRINI, A. Hæmatologica, Napoli, 1920, i, 260.

GERRONNE. Berl. klin. Wchnschr., 1906, xliii, 1154.

GIFFIN, H. Z. Trans. Assoc. Amer. Phys., 1917, xxxii, 32. Amer. Jour. Roentgenol., 1918, v, 292. Medical Record, 1918, cxiv, 1020.

GILBERT, A., ET WEIL, P. E. Arch. d. méd. exper. et. d'anat. path., Paris, 1899, xi, 157; and 1904, xvi, 163.

GRAFE, E. Deutsch. Arch. f. klin. Med., 1911, xii, 406.

GRAHAM, C. F. Jour. A. M. A., 1915, lxiv, 505.

GRAHAM, G. S. Jour. Med. Res., 1916, xxxv, 15; and 1918, xxxix, 15.

GRAM, C. Hospitalstid., Jan. 15, 1919, lxii, 77; abstr., Jour. A. M. A., April 26, 1919, lxxii, 1262.

GRAPIOLA, A. C., ET MAGLIONE, R. Rev. sud.-am. de endocrinol., Buenos Aires, 1920, iii, 195.

GRAWITZ, E. Klinische Pathologie des Blutes, Leipzig, G. Thieme, 1911.

GREENE, C. L. Medical diagnosis, 4th Ed., p. 153, P. Blakiston's Son & Co., Phila., Pa.

GUNEWARDENE, T. H. Brit. Jour. Child. Dis., London, 1920, xvii, 9-18.

GURD, F. B. Jour. Infectious Diseases, 1912, xi, 225.

HAENISCH, F., UND QUERNER, E. Ztschr. f. klin. Med., Berlin, 1919, lxxxviii, 28.

HALL, C. C., AND WHIPPLE, G. H. Amer. Jour. Med. Sc., 1911, clvii, 453.

HARRIS. American Jour. Med. Sci., 1908, lxxviii.

HARTZELL, M. B. Internat. Clinics, 1918, iv, 88.

HAUGHWOUT, F. G., AND ASUZANO, M. A. N. Y. Med. Jour., 1919, cx, 180.

HAZEN, H. H. Jour. of Cutaneous Diseases, 1911, xxix, 521.

HEAD, G. D. Minnesota Medicine, March, 1921.

HEIMANN, H. L., AND OTHERS. Lancet, London, 1918, cxcv, 879.

HEKMAN, J. Acute leukemia. Nederl. Tijdschr. v. Geneesk. Amst., 1920, 1, 1888,-1890.

HENDERSON, Y., AND EDWARDS, J. H. Amer. Jour. of Physiol., 1903, ix, 417.

HERXHEIMER, G. München. med. Wchnschr., 1913, lx, 2506; 2573.

HERZ, A. Die akute Leukemie. Leipzig u. Wien, 1911.

HIRSCHFELD, H. Ueber atypische Leukämien. Folia Hæmat., Berlin, 1904, i, 150. Zeit. f. klin. Med., 1914, lxxx, 126.

HIRSCHFELD, H., UND ALEXANDER, W. Berl. klin. Wchnschr., 1902, xxxix, 231.

HIRSCHFELD, H., UND DUNNER, L. Berl. klin. Wchnschr., 1915, lii, 9.

HIRSCHFELD, H., UND JACOBY, M. Berlin. klin. Wchnschr., 1909, xlvi, 314.

HIRSCHFELD, H., UND KOTHE, R. Deutsch. med. Wchnschr., 1907, xxxiii, 1255.

HOEFER, P. A. Centralbl. f. Bakt. u. Parasitenk., Orig., 1910, lv, 19.

HOKE, E. Prager med. Wchnschr., 1912, xxxvii, 209.

HOUDE. Thèse de Paris, 1910.

HUBER, F. Acute lymphatic leukemia. Arch. Pediatr., N. Y., 1913, xxx, 805.

INABA, I., AND OHASHI, L. Amer. Jour. Dis. Children, 1918, xvi, 1.

IRELAND, R. A., AND OTHERS. Jour. A. M. A., 1915, liv, 948.

JACKSON, J. M., AND SMITH, W. D. Boston Med. and Surg. Jour., 1915, clxxii, 136.

JACOBSTHAL, E. München. med. Wchnschr., 1910, lvii, 1036.

JACOBAEUS, H. C. Deutsch. Arch. f. klin. Med., 1909, xcvi, 7.

JOACHIM, G. Deutsch. Arch. f. klin. Med., Leipzig, 1906, lxxxvii, 437. Zeits. f. klin. Med., Berlin, 1906, lx, 27.

JOCHMAN, E., UND MUELLER, G. München. med. Wchnschr., 1906, liii, 1393.

KAST. Münch. med. Wchnschr., 1902, i, 2093.

KAUFMANN, M. Therap. Monatschr., 1915, xxix, 324.

KIRALYFI, G. Wien. klin. Wchnschr., 1912, xxv, 1311.

KLEMPERER, G., UND HIRSCHFELD, H. Therapie der Gegenwart, 1913, liv, 57.

KLIENBERGER, C. Strahlentherapie, Berlin, 1913, ii, 573.

KNOX, J. M. Arch. Pediatr., N. Y., 1915, xxxii, 392. Pediatrics, 1916, xxviii, 74.

KNUDSON, A. Boston Med. and Surg. Jour., 1917, clxxvi, 503.

KONIGER, H. Deutsch. Arch. f. klin. Med., 1906, lxxxvii, 31.

Kopanaris, P. Arch. f. Schiffs u. Tropen Hyg., 1912, xvi, 213.

Koranyi, A. v. Berl. klin. Wchnschr., 1912, xlix, 1357.

Koranyi, R. Tr. Internat. Cong. Med., London, 1914, Sect. 6, p. 79.

Korns, J. H. China Med. Jour., Sept., 1918, xxxii, 420.

Kraus, F. Zeit. f. klin. Med., 1893, xxii, 449.

Krause, P. Stizungsb. d. naturh. Ver. d. preuss. Rheinl. u. Westphal., Bonn., 1912-13, B. 24.

Kurpjuweit, O. Deutsch. Arch. f. klin. Med., 1903, lxxvii, 553.

Kurt, Z. Zeits. f. Med., Elektr. u. Roentgen Kunde, March, 1909.

Labbe, M., and Delille, A. Gazette des Maladies Infantiles, 1903, v, 97.

Larrabee. Boston Med. and Surg. Jour., Feb. 6, 1908; and 1904, cl, 540.

Lavenson, R. S. Univ. of Penn. Med. Bull., 1908, xxi, 178.

Lazarus, P., und Fleischmann, A. Deutsch. med. Wchnschr., Leipzig, 1905, xxxi, 1209,

Leisering, A. Bericht ueber das Veterinär. im Köngr. Sachsen, 1858, xxxv.

Lepehne. Deutsch. med. Wchnschr., Leipzig u. Berlin, 1919, xlv, 896.

Lereboullet, P., et Chabrol, E. Bull. et mém. Soc. méd. d. hop., Paris, 1913, xxix, 554.

Leube, W. V. Deutsch. Klinik, 1903, iii, 177.

Levin, I. Medicine and Surgery, 1917, i, 411.

Lindbom, O. Svenska läk.-sällsk. handl., June, 1919, xlv, 83; abstr. Jour. A. M. A., Aug. 30, 1919, lxxiii, 730.

Lindner, H., Deutsch. Arch. f. klin. Med., Leipzig, 1905, lxxxv, 211.

Linser, et Sick. Deutsch. Archiv. f. klin. Med., 1908, lxxxix, 413.

Loewit, M. Die Leukämie als Protozoeninfektion, Wiesbaden. J. F. Bergmann, 1900.

Longcope, W. T., and Donhauser, J. L. Jour. Exp. Med., 1908, x, 618.

Lossen, J., und Morawitz, P. Deutsch. Arch. f. klin. Med., 1905, lxxxiii, 288.

Lowenstein, A. Wien. klin. Wchnschr., 1918, xxxi, 1025.

Ludke, H. Deutsch. Arch. f. klin. Med., 1910, c, 552. Deutsch. med. Wchnschr., Leipzig, 1920, xlvi, 345.

McCrae, T. Brit. Med. Jour., 1905, i, 407. Johns Hopkins Hosp. Bull., 1900, xi, 102.

McJunkin, F. A. Jour. A. M. A., 1920, lxxiv, 17.

Macht, D. I. Jour. of Pharm. and Exp. Therap., 1918, ii, 419.

Mager, W., und Sternberg, C. Wien. klin. Wchnschr., 1906, xix, 1471.

Magnus-Levy, A. Virchow's Arch. f. path. Anat., 1898, clii, 107.

Mallory, F. B. The principles of pathologic histology. Philadelphia, Saunders, 1914.

Mariani, G. Gior. ital. d. mal. ven., Milano, 1920, lxi, 63.

Marmol, D. B. Vida Neueva, Havana, 1919, xi, 123.

Marshall, M. Arch. Int. Med., Chicago, 1915, xvi, 1045.

Martelli, C. Gazz. internaz, di med., Napoli, 1919, xxii, 293, 312; and 1920, xxiii. 3-5. Pediatria, July, 1919, xxvii, 385; abstr. Jour. A. M. A., Sept. 6, 1919, lxxiii, 799.

Martin, C. F. *In* Forchheimer's Therapeusis of Internal Diseases, Vol. III, 844.

Masing, E. Deutsch. Arch. f. klin. Med., Leipzig, 1908, xciv, 377.

Menetrier, et Touraine. Arch. mal. du Coeur, Feb., 1911.

Meyer, E. Münch. med. Wchnschr., 1903, i, 1489.

Milroy, T. H., and Malcolm, J. Jour. of Physiol., 1898, xxiii, 217.

Mimerbi, et Prampolini. Priv. Crit. di Clin. Med., April 13, 1907; synop. Arch. Mal du Coeur, 1908, 327.

Moraczewski, W. v. Arch. path. Anat. u. Physiol., 1898, clix, 221.

Morawitz, P. Deut. Arch. f. klin. Med., 1906, lxxxviii, 503.

Morelli, G. Wien. Vrtljschr. f. Zahnh., 1920, xxxvi, 103.

Moreschi, C. Zeit. f. Imm. Forsch. u. Exp. Therap., 1914, Orig., xxi, 410.

Morris, R. S., and Boggs, T. R. Arch. Int. Med., 1911, viii, 806.

Muck, E. Cor.-Bl. f. schweiz. Aertze, Dec. 14, 1918, xlviii, 1671; abstr. Jour. A. M. A., Feb. 15, 1919, lxxii, 528.

Muir, R. Leukemia. *In* Allbutt and Rolleston's System of Medicine, London, 1909, Vol. V, 788.

Muller, H. F. Deutsch. Arch. f. klin. Med., Leipzig, 1891, xlviii, 47.

Munro, E. E. H. Jour. A. M. A., 1920, lxxiv, 603.

Murphy, J. B., Means, J. H., and Aub, J. C. Arch. Int. Med., 1917, xix, 890.

Musser, J. H., and Edsall, D. L. Univ. of Penn. Med. Bull., 1905, xviii, 174.

Naegeli, O. Leukemie und Pseudoleukaemie. Als zweite Auflage des Werkes von P. Ehrlich, A. Lazarus u. F. Pinkus, Wien u. Leipzig, 1913, A. Holder, p. 234. Ergebn. d. inn. Med. u. Kinderh., Berlin, 1910, iv, 222. Blutkrankheiten u. Blutdiagnostik. Veit u. Co., 1912. Therap. Monatsch., February, 1910.

Nakamura, H. Deutsch. Zeits. f. Chir., Leipzig, 1914, cxxxii, 275.

Nanta, A. Arch. d. mal. du. Coeur, 1913, vi, 38.

Nanta, et Loubet. Folia Hæmat., 1913, xvi, 75.

Neumann, E. Arch. d. Heilk., Leipzig, 1870, xi, 1.

Nihonmatsu, T. Verhandl. d. Japan, path. Gesell., Tokio, 1916, vi, 126.

Noble, T. H. Indianapolis Med. Jour., 1920, xxiii, 422.

Nocard, E. De la Leucocythémie chez les animaux domestiques. Paris, 1881.

von Noorden, C. Therap. Monatshr., 1914, xxviii, 23.

von Noorden, C., und Falta, W. Med. Klinik., 1911, vii, 1487.

Oettinger, Fessinger, et Sauphar. Arch. mal du Coeur, May, 1910, 273; synop. Folia Hæmat., July, 1910.

Oliveri, G., y Mazza, S. Gazz. d. osp., Milano, 1920, xli, 229.

Oppenheim, E. A. Virchow's Arch. f. path. Anat., 1911, xxiv, 392.

Ordway, T. Trans. Assn. Amer. Phys., 1916, xxxi, 177.

Ordway, T., and others. Albany Med. Annals, 1920, xli, 1.

Ordway, T., and Gorham, L. W. Oxford Medicine, Vol. II, 681.

Ordway, T., and Kellert, E. Jour. Med. Research, 1913, xxviii, 287.

Osler, Sir W. Practice of medicine, 8th Ed., p. 741, D. Appleton & Co., New York.

Packard, M., and Ottenberg, R. Jour. A. M. A., 1917, lxviii, 954.

Paltauf, R. Ergevnisse d. Path. u. Anat., 1896, iii, 652.

Pancoast, H. K. Amer. Jour. Roentgen., 1917, iv, 611. Therap. Gazette, Detroit, 1908, 3. s., xxiv, 533.

Panton, P. N., und Tidy, H. L. Folia Hæmat., Leipzig, 1913, xvi, 75; and 1913, xvii, 398.

Pappenheim, A. Die Zellen der leukämischen Myelose (Leukämie-Zellen). Jena, 1914. Berlin. klin. Wochen., 1908, xlv, 60. Folia Hæmat., Leipzig, 1907, iv, 1-53, 141-201, 329-388, 535-602. Pathologie u. Therapie der Leukämie, Folia Hæmat., Leipzig, 1909, vii, 346. Folia Hæmat., July, 1910, x, 1.

Pappenheim, A., und Hirschfeld, H. Folia Hæmat., 1908, v, 347.

Parvu, M. Comptes Rend. de la. Soc. de Biol., 1908, lxv, 480.

Peabody, F. W. Boston Med. and Surg. Jour., 1917, clxxvii, 873.

Peacock, A. H. Amer. Jour. Med. Sc., 1904, cxxviii, 893.

Petit, J. Normandie méd., Rouen, 1919-20, xxxi, 176.

Peutz, J. L. A. Nederlandsch. Tijdschr. v. Geneesk., March 1, 1919, i, 655; abstr., Jour. A. M. A., May 17, 1919, lxxii, 1503.

Pinch, A. E. H. Brit. Med. Jour., 1915, i, 367.

Pinkus, F. Arch. f. Dermat. u. Syph., Wien u. Leipzig, 1899, i, 37, 177.

Pirie. Brit. Jour. of Tuberculosis, April, 1908.

Pisek, G. R. Arch. of Pediatrics, 1916, xxxiii, 938.

Pollitzer, H. Wien. med. Wchnschr., 1919, lxix, 799.

Pribam, B. O., und Rosky. Zeitschr. f. exper. Path. u. Ther., vi, 1909, 7-24; synop. in Folia Hæmat., July, 1910.

Pribam, B. O., und Stein, B. Wien. klin. Wchnschr., 1913, xxvi, 2021.

Querner, und Haenisch. Deutsch. med. Wchnschr., 1916, xlii, 1209.

Ravenna, F. Gior. de clin. med., Parma, 1920, i, 45-50.

Renon, Degrais, and Dreyfus, L. Trans. Internat. Cong. Méd., London, 1913.

Renon, Degrais, et Tournemelle. Bull. et mém. de la Soc. méd. des hôpitaux de Paris, 1914, xxxvii, 526.

Reschad, Hasson, und Schilling, V. München. med. Wchnschr., 1913, lx, 1981.

Roessingh, M. J. Nederl. Tijdschr. v. Geneesk., Amst., 1920, ii, 508.

Rolleston, J. D. Proc. Roy. Soc. Med., 1914, vii, 1.

Rolleston, H. D., and Rolleston, J. D. Brit. Jour. Child. Diseases, London, 1915, xii, 33.

Rosenthal, E. Berl. klin. Wchnschr., 1919, lvi, 1113-1116.

Roth, O. Ztschr. f. klin. Med., 1913, lxxviii, 75.

Rotky, H. Zentralbl. f. innere Med., 1914, xxxv, 953.

Ruh, H. O. Cleveland Med. Jour., 1912, xi, 859.

Ryan, E. R. U. S. Nav. M. Bull., April, 1919, xiii, 297.

Ryan, M. L. Jour. A. M. A., Feb. 15, 1919, lxxii, 472.

Scheuer, O. Arch. f. Dermat. u. Syph., 1911, cix, 449.

Schmeisser, H. C. Jour. Exper. Med., Lancaster, Pa., 1915, xxii, 820. Johns Hopkins Hosp., Reports, 1919, xviii, 24; and 1916, xvii, 551.

Schnyder, K. Cor.-Bl. f. schweiz. Aerzte, Jan. 4, 1919, xlix, 18; abstr. Jour. A. M. A., March 1, 1919, lxxii, 687.

Schultze, W. H. Münch. med. Wchnschr., 1909, lvi, 167.

Saphier, J., und Seyderhelm. München. med. Wchnschr., 1920, lxvii, 69.

Sappington, S. W. Amer. Jour. Med. Sci., 1916, clii, 238.
Sellards, A. W., and Baetjer, W. A. Johns Hopkins Hosp. Bull., 1918, xxix, 135.
Selling, L. Beitr. z. path. Anat. u. z. allg. Path., Jena, 1911, li, 576. Johns Hopkins Hosp. Reports, 1916, xvii, 83. Johns Hopkins Hosp. Bull., 1910, xxi, 33.
Sequeira, J. H. Proc. Roy. Soc. Med., London, 1918-19, xii, Sect-Dermat., 54.
Seyderhelm, R., und Kratzeisen, E. Zeit. f. klin. Med., Berlin, 1919, lxxxviii, 161.
Shapiro, L. G. Proc. N. Y. Path. Soc., 1919, n. s., xix, 73.
Simon, C. E. Amer. Jour. Med. Sc., 1907, cxxxiii, 390.
Simon, C. E., and Judd, C. C. Jour. A. M. A., 1915, lxiv, 1630.
Simon, W. V. Berl. klin. Wchnschr., 1912, xlix, 893.
Sohn, I. Wien. klin. Wchnschr., 1913, xxvi, 573.
Steele, A. E. Boston Med. and Surg. Jour., 1914, clxx, 125.
Stejskal, C., und Erben, F. Zeit. f. klin. Med., 1900, xxxix, 151.
Stengel, A., and Pancoast, H. K. Jour. A. M. A., 1908, l, 1317.
Stenstrom, O. Ztschr. f. Imm. Forsch., 1911, viii, 483.
Sternberg, C. Wien. klin. Wchnschr., 1920, xxxiii, 553. Wien. klin. Wchnschr., 1911, xxiv, 1624. Ziegl. Beitr. z. path. Anat. u. all. Path., 1905, xxxvii, 437; and 1915, lxi, 75.
Stevens, J. L. London Lancet, 1902, ii, 792.
Strauch, A. Amer. Jour. Dis. Children, 1913, v. 43.
Stursberg, H. Med. Klin., 1912, viii, 520.
Sweitzer, S. E. Jour. A. M. A., 1916, lxvii, 1511.
Symmers, D. Jour. Path. and Bact., 1905, x, 159.
Tapie, J., et Cassar, A. Arch. d. mal. du Coeur, May, 1919, xii, 218.
Taussig. Interstate Med. Jour., 1908, xv, 439.
Thaler, H. Zentralbl. f. Gynäk., Leipzig, 1920, xliv, 436.
Toenniessen, E. München. med. Wchnschr., 1920, lxvii, 1059.
Tschistovitch, et Arinkine. Comptes rend. de la Soc. de Biol., 1913, lxxiv, 147.
Turk, W. Wien. klin. Wchnschr., 1907, xx, 158; 1903, xvi, 1073; and 1913, lxiii, 625
Tyzzer, E. E., and Ordway, T. Jour. Med. Research, 1909, xxi, 459.
Vanderwey, H. Deutsch. Arch. f. klin. Med., 1896, lvii, 287.
Vas. Ztschr. f. klin. Med., 1909, lxix.
Virchow, R. Froriep's Notizien, 1845, No. 780. Med. Ztschr., 1846 xv, 157. Virchow's Archiv., 1853, v, 43.
Vogel, J. Arch. f. Path. Anat., Berlin, 1851, iii, 570.
Vollenweider, P. Ueber familiäres Auftreten von angeborener Leukämie (Zurich), Thalwil, 1914, F. Tellenbach.
Walterhofer, G. Berl. klin. Wchnschr., 1920, lvii, 589.
Ward, G. R. London Lancet, 1914, i, 1459. Brit. Jour. Child. Dis., London, 1920, xvii, 18; and 1917, xiv, 10. Proc. Roy. Soc. Med., 1913, vii, Medical Section, 126.
Warthin, A. S. Trans. Internat. Cong. Med., 1913, London, 1914, Sec. III, Gen. Path. and Path. Anat., Part 2, 313. Amer. Jour. Med. Sci., 1914, cxlvii, 72. Internat. Clin., 1906, iv, 243; and 1907; synop. in Folia Hæmat., 1909, viii, 1. Internat. Clin., 1909, iv, 280.
Weber, F. P. Quart. Jour. Med., 1919, xii, 212.
Wells, H. G. Trans. Assn. Amer. Physicians, 1916, xxxi, 170.
White, H. Guy's Hospital Gazette, 1913, xxviii, 421.
White, W. H., and Hopkins, F. G. Jour. of Physiol., 1899, xxiv, 42.
Wickham, L. F., et Degrais, P. Radiumtherapie. Paris, J. B. Bailliere et fils, 1909.
Wilbur, R. L. Jour. A. M. A., 1915, lxv, 1255.
Wilkinson, R. Lancet, 1903, i, 1739.
Winkler, F. Folia Hæmat., 1907, iv, 323.
Winternitz, M. C., and Schmeisser, H. C. Johns Hopkins Hospital Reports, 1919, xviii, 25.
Wirth, D. Monatscha. f. prakt. Tierh., Stuttg., 1920, xxxi, 97.
Wynhausen, O. J. Deutsch. Arch. f. klin. Med., 1908, xcii, 497.
Ziegler, C., und Jochmann, G. Deutsch. med. Wchnschr., Leipzig u. Berlin, 1907, xxxiii, 749.
Ziegler, K. Experimentelle u. klin. Untersuchungen ueber die Histogenese der myeloiden Leukämie. Jena, 1906, G. Fischer.

CHAPTER IV

OTHER BLOOD DISEASES

By Charles Lyman Greene, M.D.

Hemophilia (hemorrhagic diathesis, hematophilia, blutkrankheit, hemophil), p. 855:—Definition, p. 855; Etiology, p. 855; Symptomatology, p. 856:—Clinical history, p. 856; Coagulation time, p. 856; Hemorrhage into joints, p. 857; Physical findings, p. 857; Laboratory findings and special examinations, p. 857—Diagnosis, p. 857; Treatment, p. 858; Prognosis, p. 859.
Purpura, p. 859:—Definition, p. 859:—Comment, p. 859;—Complicating purpuras, p. 859; Arthritic purpuras, p. 860:—Peliosis rheumatica (Schönlein's disease), p. 860; Henoch's purpura, p. 860—Simple purpura, p. 860; Purpura hemorrhagica, p. 860; Fulminating purpura, p. 860.—Etiology, p. 861; Symptomatology, p. 861; Diagnosis, p. 861; Treatment, p. 862; Prognosis, p. 862.
Polycythemia, p. 862:—Definition, p. 862.
Erythremia, p. 863:—Definition, p. 863; Etiology, p. 863; Symptomatology, p. 863; Clinical varieties, p. 865; Treatment, p. 865; Prognosis, p. 865; Pathology, p. 865.

HEMOPHILIA

(Hemorrhagic Diathesis, Hematophilia, Blutkrankheit, Hemophil)

Definition.—This is a morbid state of unknown causation, familial and hereditary, transmitted by the female only (whom it spares) to two-thirds of the male offspring, associated with a deficiency of prothrombin in the circulating blood with blood-platelets of deficient prothrombin productivity, consequent delayed coagulation, and a life-long tendency to serious or fatal hemorrhage, spontaneous or induced.

Comment.—In the case of from 25 to 30 per cent. of the females of such families there is no conduction of the hemophilia, their sons wholly escaping the familial stigma.

Etiology.—Aside from the condition stated in the definition, the etiology of hemophilia remains a mystery. It unquestionably is a matter of inherent predisposition expressed possibly both in deficient structure and impaired function. A large number of causes have been advanced, such as calcium deficiency, a peculiar thinness and fragility of the vessel walls, abnormal alkalinity of the blood, a neuropathic tendency, and the like, but the only features at present of importance are those stated in the opening paragraph.

Age and Sex.—It affects chiefly male children under ten years of age, first appearing oftentimes in early childhood and occasionally manifesting itself in infancy or even at birth. It has been stated that one having to do with families suffering from this taint may be able to detect in the manner of bleeding at birth when the cord is cut a tendency to hemophilia in the individual babe even though the hemorrhage at that time is not excessive. In such of those affected as live to maturity the tendency seems to diminish gradually with increasing age and may disappear almost wholly in the advanced years of life.

The oft-repeated claims that women of hemophilic stock may themselves be bleeders seems to be unsupported by substantial evidence. Such women of a tainted family as are unfortunate enough to transmit this morbid tendency to the majority of their male offspring serve apparently only as conductors. Unfortunately, it would appear that their fecundity is peculiarly great and further that male predominance is decided in their children. Similarly, the claim that transmission occurs occasionally through the male seems to have been wholly disproved by a very careful study of reported cases.

Symptomatology.—CLINICAL HISTORY.—As stated, this condition presents itself usually and almost invariably in early childhood, often in the first year of life, and in rare instances at birth when severe or even fatal hemorrhage may follow the severing of the umbilical cord. There are no premonitory symptoms in the older children or other individuals who develop the disease and in most instances the detection of the condition depends upon the occurrence of more or less intractable or greatly prolonged hemorrhage, spontaneous or induced.

There is no doubt that hemorrhage may occur in these individuals without any wound or decided contusion even, but in many instances there has been some excessive pressure or mild injury which may not have broken the skin yet be adequate to cause bleeding. The commonest site of hemorrhage is the mucous membrane of the nose and such attacks of epistaxis are relatively frequent and most difficult to control.

Similarly, hemorrhage apparently spontaneous may arise from the throat, gums, lips, buccal mucous membranes, stomach, lungs, bowel, urethra, or, in the female, from the uterine or vaginal mucous membranes. The danger from cuts or abrasions of any sort is manifest and many instances are on record where such tainted individuals have bled to death from very slight operative procedures such as the extraction of a tooth.

In most instances,of course, the hemophilic tendency of the individual is well known to the family members and he is safeguarded to the utmost possible extent and will bring usually to the physician information of his morbid tendency. Nevertheless, in many instances, for some reason this information has been suppressed and serious consequences have followed operative procedure unwittingly undertaken by the surgeon.

COAGULATION TIME.—The coagulation time is greatly prolonged in this disease although this varies greatly in duration and at times may be nearly or quite normal. This fact explains the apparent temporary immunity of hemophilic individuals such as every physician may have noted. Another matter of interest in this connection is the extraordinary rapidity with which blood regeneration occurs in such patients after most severe, exhausting, and extreme hemorrhages.

Instead of a normal coagulation time the bleeding in the case of these afflicted individuals may continue uninterruptedly for hours without the slightest tendency for a clot to form if there is an open wound. The circulating blood in them behaves in a manner wholly opposite to that of blood mixed with the tissue juices which, by reason of its cephalin content perhaps, seems to promote coagulation.

Hemorrhage into the Joints.—The possibility of hemorrhage into the joints, pleuræ, pericardial sac, and in fact almost any cavity of the body, actual or potential, should be borne in mind. The persistent or long-continued hemorrhages between articular surfaces result in their destruction and in very marked deformity.

Physical Findings.—These are wholly negative save in the presence of actual hemorrhage or in the residual signs of a recent attack.

Laboratory Findings and Special Examination.—The blood-picture in these cases is ordinarily nearly normal unless there is a history of recent severe or recurrent hemorrhage and even in such instances, owing to the rapid blood regeneration, the blood-picture gives little information after any considerable time has elapsed.

Howell has demonstrated that in hemophilic blood, although there is a shortage of prothrombin, that present seems to be qualitatively active. He feels, therefore, that the lengthened coagulation time in the case of hemophilics is due to a prothrombin shortage in the circulating blood only, and others have demonstrated that the platelets, if they are present in normal numbers, ordinarily are deficient in prothrombin-producing activity.

The tests for coagulation time and prothrombin activity and sufficiency as made by Howell embody the following procedure:

A sufficient quantity of blood is taken from the vein, with due precaution to exclude any avoidable bruising or injury of the surrounding tissues. Six cubic centimeters (1.62 fluidrams) of the blood so obtained are used. Two cubic centimeters (32.4 minims) are poured into a small test-tube which is carefully inclined at intervals thereafter in order to note any tendency to fixation by clotting. This is considered complete when the tube can be wholly inverted. Under this method normal blood should clot within a period of from 20 to 30 or 40 minutes.

The remaining 4 c.c. (64.0 minims) of blood under test are placed in a centrifugalization tube and 0.05 c.c. (.80 minim) of a 1 per cent. oxalate solution in 0.9 per cent. sodium chlorid are added. After thoroughly mixing the specimen is centrifugalized at high speed for from 20 to 30 minutes and the clear plasma result is removed with a pipette. In each of four tubes 5 drops of this plasma so obtained are placed and to these respectively are added 2, 3, 4 and 5 drops of a 0.5 per cent. solution of calcium chlorid.

The shortest coagulation time thus obtained is compared with that observed in a control series prepared in exactly the same manner from normal blood. Howell states that normal blood plasma so tested clots in from 9 to 12 minutes, whereas the clotting time in the case of hemophilic blood-plasma varies from 2 to 5 hours.

Diagnosis.—The diagnosis in hemophilia is in most instances rendered easy by the known and stated fact that the individual under observation comes from tainted stock. In cases where no definite informataon is obtainable, error is most likely to arise in connection with purpura hemorrhagica; much less so in cases of leukemia where the physical findings and the clinical signs quite apart from the blood-picture should be sufficient to prevent confusion.

In the case of purpura hemorrhagica it should be remembered that the blood-platelets are greatly reduced whereas in hemophilia they are normal or approximately so in number. As a matter of fact in clinical practice hemophilia is usually a clearly-defined outstanding condition and little difficulty in diagnosis is experienced.

Treatment.—Prevention of hemorrhage occupies first place in the treatment of this disease and this, of course, means that all male children of tainted stock must be protected most carefully from wounds and abrasions alike. As the child grows older he should be informed of his inherited tendency and be taught to protect himself in every way possible. In this way only a limited amount of security can be obtained as obviously in childhood and maturity alike open wounds, abrasions and bruises cannot be escaped.

In an actual attack the patient should be kept as **quiet** as possible and relieved so far as may be of fear and nervous disturbances. In many instances it is wise to give small doses of an **opiate** in order to do away with the dread of impending death which so many of these patients very naturally experience.

It is hardly necessary to state that in hemophilic children or children that are believed to be tainted, even the most trivial operations should be avoided so far as is humanly possible. This fact was recognized by the ancient Jews in relation to the rite of circumcision, and even at that time there were rules laid down evidently intended to protect individuals of this class. In any event, before operation of any sort is attempted the coagulation period should be accurately determined.

It will be understood readily that practically all of the surgical means usually employed to control hemorrhage, such as ligation of vessels, cauterization, application of pressure, and the like, will prove wholly futile; this by reason of the fact that the bleeding is merely a capillary oozing of a peculiarly persistent type. **Styptics** may be used and in certain instances seem to have had some favorable effects. The same may be said of the use of strong solutions of **cocain** and **adrenalin chlorid.** The objection to this last procedure is obvious, however, in that if the hemorrhage is not wholly controlled within a short time the after-effect of the drug will be such as to promote relaxation of the vessels and an aggravation of the original hemorrhage.

Jay McLean and others have strongly recommended the use of **cephalin,** a substance obtained from the tissue juices, which is probably responsible for the prompt clotting of hemophilic blood when accidentally mixed with such juices. McLean emphasizes the fact that cephalin loses its thromboplastic power if exposed to the air and states that after an interval of two or three months it becomes wholly worthless. Obviously, therefore, a fresh specimen should be prepared wherever possible and kept in vacuo. Hynson, Westcott & Dunning, of Baltimore, carry surgical gauze which has been saturated in a concentrated ether solution of cephalin, sterilized and placed promptly in sterile glass tubes which are sealed after the contained air is wholly exhausted. It is said that this material remains thromboplastically active for at least three years. If this preparation is unavailable, the use of gauzy compresses which have been saturated in fresh normal blood-serum should be tried whenever practical.

Various forms of serum injections have been used with some degree of success in these cases but it is wiser probably to resort to transfusion of the whole blood carried out in the usual manner. The gelatine treatment of Sahli, which enjoyed quite a vogue for several years, seems to have been wholly abandoned and at the present time is not credited with any decided beneficial results. The internal administration of cephalin has been attempted, apparently without convincing results, although improvement in the coagulation time has apparently occurred in certain instances.

Prognosis.—The mortality in this disease is extremely heavy and the majority of the male children of affected families die under ten years of age. As has been stated previously, certain children of tainted stock escape wholly and in the case of other individuals the disease appears only in a mild form. The immediate prognosis in a case of severe hemorrhage is always a grave one and up to the present time very little has been done effectively to control such hemorrhages.

PURPURA

Definition.—Purpura is a morbid state characterized in its graver forms by a low blood-platelet count, prolonged bleeding time, deficient contractility of the blood-clot without delayed coagulation time, and by hemorrhages, subcutaneous, and submucous, from free mucous membranes, or, in rarer instances, an outpouring of blood into the serous cavities. A deficiency of blood-platelets and the consequent lack of thrombo-forming material accounts no doubt for the persistent or greatly prolonged bleeding time noted in the severer forms of purpura.

The cause of platelet deficiency is wholly unknown, nor can one determine whether in any given case the unknown causative factor operates so as to destroy them when formed, inhibit their production from the megacaryocyte, or destroy the parent cell in the bone marrow. The platelet count has a practical value in this ailment inasmuch as a count below 60,000 per cubic millimeter predisposes to or initiates hemorrhage from the mucous membrane (Minot), and with a decided rise in the count the danger of hemorrhage disappears. In severe purpura the platelets may be reduced to 5,000 or less per cubic millimeter of blood, which figure represents an almost complete disappearance of these vitally important elements.

COMMENT.—So little of positive information exists with respect to this disease save as to its clinical variants that an arbitrary classification is justified only on the ground of clinical convenience. It bears a close resemblance to certain forms of urticaria, scurvy, hemophilia, and to the exudative forms of an erythematous nature in general. It possesses actually but two constant and invariable symptoms, namely, imperfect thrombus formation and subcutaneous hemorrhages. Cases may be grouped conveniently under five general heads:

1. Complicating purpuras.
2. Purpuras with arthritic manifestations.
3. Simple purpura.
4. Purpura hemorrhagica (morbus Werlhofii).
5. Purpura fulminans.

COMPLICATING PURPURAS.—Under this head we deal with (*a*) the purpuras associated with acute infections, and (*b*) those occurring in the course of chronic diseases associated with cachexia. When purpura occurs in association with acute infection, it ordinarily indicates an exceptionally severe type of the disease. One may encounter it in typhoid fever, smallpox, malignant endocarditis, septicemia, pyemia, whooping-cough and measles as well as in the more virulent of the tropical diseases. In cerebrospinal meningitis and typhus fever it represents the usual exanthem.

In the chronic diseases it is seen most frequently in connection with scurvy, pernicious anemia and leukemia, not infrequently in tuberculosis, Bright's disease, Hodgkin's disease, syphilis, and various cardiac lesions, particularly those associated with marked degeneration of the myocardium. In epilepsy it is not uncommon and sometimes points the way to a correct diagnosis in cases of an obscure nocturnal type. In such instances it is usually slight and transient, often showing only on the face as an indistinct capillary streaking which may last for a few hours or a few days.

In hysteria, the same form may be present, or the rarer forms, among which the most curious is the cruciform purpura in which, it is said, the hemorrhages appear at points corresponding to the wounds of the Saviour on the cross. It may be seen at once that in epilepsy and whooping cough mechanical strain plays a great part. True purpura would seem to be a more or less direct expression of an infection and might better be considered wholly apart from the conditions mentioned in the paragraph preceding.

ARTHRITIC PURPURAS.—Under this heading two types exist, namely, (*a*) peliosis rheumatica, and (*b*) Henoch's purpura.

Peliosis Rheumatica (Schönlein's Disease).—This ailment is characterized by a joint involvement more or less severe and corresponding very closely to the ordinary type of an acute multiple arthritis. Sore throat usually precedes the attack and purpuric manifestations of a cutaneous nature constitute the most striking and outstanding symptom. Not only are there subcutaneous and perhaps submucous hemorrhages but purpuric edema and marked urticarial manifestations or even pemphigoid lesions may be present. The disease is febrile and runs a variable course; ordinarily the temperature range does not exceed 103° F. (39.44° C.).

The actual joint involvement as a rule is not very severe, though the pain may be extreme prior to the oncoming of the cutaneous manifestations. The tendency to relapse in this ailment is one of its peculiarities and in several instances observed by the author the return was annual and fell at about the same time each year.

Henoch's Purpura.—This is the name given to a more severe form of the disease in which the gastro-intestinal symptoms, such as nausea, vomiting, diarrhea, and hemorrhages from the mucous membranes, constitute features of such predominance as to obscure or lessen the importance of the accompanying joint manifestations. In cases of this type not only albuminuria but an actual acute nephritis may occur and the visceral crises may invite totally unwarranted surgical interference.

SIMPLE PURPURA.—Cases are occasionally encountered in which without any apparent cause purpuric skin manifestations develop without marked constitutional symptoms and either lacking entirely joint involvement or possessing this symptom only in a minor and trifling degree.

PURPURA HEMORRHAGICA (MORBUS WERLHOFII).—This terrible disease may be rapidly fatal and is characterized by severe and often intractible hemorrhage from any and all mucous membranes, and is associated with high fever.

FULMINATING PURPURA.—In this form the disease runs a rapidly fatal course and may terminate without the appearance of joint lesions, those of the skin being the only striking indications of the nature of the ailment.

Etiology.—Age and Sex.—With respect to age and sex there are no figures of sufficient completeness on which to base positive statements, but simple purpura occurs chiefly but not exclusively in young children, peliosis rheumatica in young adults for the greater part, whereas purpura hemorrhagica occurs chiefly in young female children.

Practically nothing is known as to the ultimate cause of purpura hemorrhagica, but, as stated in a previous paragraph, there is a diminution in the number of the blood-platelets present which indicates that this feature of the ailment determines the occurrence or nonoccurrence of hemorrhages. If then we consider the frequency with which a probable cause is present in the complicating purpuras, we are led to assume the possibility at least that even in the apparently idiopathic forms, such as so-called simple purpura and purpura hemorrhagica, we are dealing either with some undiscoverable infectious agent or some equally elusive toxin which operates to prevent the formation of blood-platelets in normal numbers.

The occurrence of purpuric manifestations in septicemia, typhus fever, malignant endocarditis, and in certain of the more violent forms of smallpox, scarlet fever and even measles, shows that in such instances the infectious agent is of peculiar virulence.

On the other hand, with respect to the toxic purpuras we find most violent poisons, such as snake venom, operating to produce a purpuric skin manifestation; and again we encounter them in association with drugs which are relatively innocuous, such as the iodids and quinin amongst others. Purpura occurring in the cachexias is more readily understood if we study the anemias occurring in the same conditions and note the readiness with which serious blood changes of an hemolytic nature not infrequently occur. The so-called "mechanical" purpuras such as result from extreme stasis in severe paroxysms of whooping cough, and in epileptic seizures are, of course, readily understood.

In the case of the so-called arthritic purpuras it would seem probable that the primary cause of the manifestation is identical with that of acute rheumatism, although the author is not aware that this is definitely proven. The so-called visceral crises which occur in connection with the severer forms of purpura, and notably in Henoch's gastro-intestinal and the arthritic types, are not easily explainable. Sir William Osler has called attention to the similar attacks occurring in angioneurotic edema and in the erythemas and urticaria. The hysterical form referred to in a preceding paragraph remains inexplicable, nor do we know exactly how the subcutaneous hemorrhages occurring in connection with locomotor ataxia and myelitis are brought about.

Symptomatology.—This has already been covered for the greater part in the running descriptions of the various manifestations of purpura.

Diagnosis.—Few diseases are easier to diagnosticate, inasmuch as the striking manifestation in the shape of a skin lesion or apparently spontaneous hemorrhage in the absence of a complicating disease, acute or chronic, makes matters clear in most instances. In peliosis rheumatica the combination of joint lesions and profuse purpuric rash is distinctive. Simple purpura offers no difficulties, nor does the fulminating type.

In Henoch's purpura the chief danger lies in the misconstruction of the pains associated with visceral crises which may precede the typical hemorrhagic manifestations. In purpura hemorrhagica one has to consider the differentiation of scurvy which is easily eliminated by reason of the lack of the peculiar changes in the gums characteristic of that disease.

Hemophilia is usually to be ruled out by virtue of the family history, its occurrence in the male only, delayed coagulation time, normal platelet count, and because in the forms of purpura of any such grade of severity as would suggest hemophilia, fever of a more or less high grade is present in most instances. In all cases, however, of this sort an examination of the blood should be made and particular attention should be paid to the counting of the blood-platelets.

Treatment.—The treatment of the purpuras is purely **symptomatic.** The severer forms of purpura are peculiarly and often permanently benefited by **transfusion** and any or all of the measures suggested under hemophilia may be used in this disease.

Prognosis.—In the milder cases of purpura spontaneous recovery occurs but there is usually a strong tendency to the occurrence of relapses, and, in the longer continued cases, to remissions and exacerbations. In Henoch's purpura of the gastro-intestinal form the mortality is said to be under 10 per cent. Fulminating purpura is almost invariably rapidly fatal. No reliable figures exist relating to the mortality in purpura hemorrhagica, but a large majority of the cases recover after an illness varying from one to four or five weeks.

POLYCYTHEMIA

(Erythrocytosis)

Definition.—This is a clinical condition characterized by a slight, decided, or striking and excessive increase of the red blood-cells of an individual above the normal count. The condition may be transient or permanent, trivial or grave, relative or absolute. When the condition is absolute, permanent and associated with persisting splenomegaly it is termed "erythremia" and will be described separately under that heading. An increase of the number of erythrocytes above the normal count of 5,000,000 per cubic millimeter may arise under many and varied conditions. Save in the relatively rare instances in which "erythremia" proper exists, the condition does not constitute a disease but may be either the reflection of diseased processes within the body or merely a physiologic response to tissues needs resulting from some peculiarity of environment.

Relative polycythemia, the common type, may represent mere blood concentration such as would result from an excessive loss of fluid or it may occur because of stasis and localized concentration of erythrocytes in the circulatory channels. Absolute polycythemia is "erythremia," a relatively uncommon, wholly distinct, slowly progressive and ultimately fatal disease.

It is probable that cases occur in which a more or less constant and persistent excess of red blood-cells is due to wholly secondary bone marrow hyperplasia. It would seem wiser to refrain from the use of the term "absolute polycythemia" as applied to such secondary cases and reserve it for use in connection with splenomegalic erythremia.

Polycythemia usually represents nothing more than blood concentration or stasis and in high altitudes is perfectly accounted for by the assumption that Nature meets an actual need associated with the rare air and the dyspnea first produced in a nonhabituated person.* This assumption is borne out by the secondary partial reduction noticed in those who take up permanent residence.

A similar slight increase may follow baths, hot or cold, massage, violent exercise and the administration of certain drugs or may be associated with the process of digestion, blood regeneration, vomiting, profuse sweating, the removal of exudates, profuse diarrheas and, it is said, with myxedema and acute yellow atrophy.

Its presence in connection with circulatory stasis, such as may occur in organic heart disease, emphysema, stenotic dyspnea and similar conditions affecting the circulation is readily understood and in extreme cases the count may reach 7,000,000 per cubic millimeter. In congenital heart disease of extreme cyanotic types the erythrocyte count may exceed 9,000,000 per cubic millimeter of blood and hyperplasia of the red marrow is found in such cases.

ERYTHREMIA

("Erythrocytosis Megalosplenica," "Absolute Polycythemia with Splenic Enlargement," "Vaquez's Disease," "Osler's Disease," "Polycythemia Vera," "Polycythemia Rubra," etc.)

Definition.—This is a slowly and intermittently progressive, ultimately fatal disease characterized by a striking and often excessive increase of the red cells, splenic enlargement usually decided or extreme, a peculiar red cyanosis, a decided or great increase in the total blood volume, hyperviscosity, shortened coagulation time and frequently by demonstrable hepatic enlargement.

Etiology.—The cause is wholly unknown. Some cases apparently are familial and congenital, other members of the family showing abnormally high counts but remaining usually symptom-free otherwise.

Symptomatology.—The disease is insidious in its development and its victims may be wholly unconscious of its presence until their attention is called or attracted to the peculiar red cyanosis of the skin and mucous membranes, so marked and characteristic of the established disease. The patient usually consults the physician because of failing reserve, lassitude or even a somewhat rapidly developed state of actual exhaustion.

In one case seen by the author, bilateral exophthalmos was the first symptom noted and not infrequently eye symptoms such as recurring or persistent dimness or blurring of the vision, "spots before the eyes" may be among the troublesome disturbances noted by the patient. Gastrointestinal symptoms are inconstant and variable in character and degree. Constipation is relatively common; anorexia may be recurrent or persistent, and cases associated with vomiting seizures are encountered. The last may be wholly unassociated with the ingestion of food and in two of the author's patients painful seizures maximal in the epigastrium occurred irregularly.

---

* An immediate primary apparent increase such as occurs in the military observers and fighters of the aviation corps is caused probably by cardiovascular embarrassment and irregularities of distribution, violent and abrupt transitions from sea level to 14,000 ft. altitude being common events of the day's work.

Epigastric oppression and flatulence are relatively common occurrences. Hemorrhage from the nose, gums, stomach or bowels has been reported but in a series of 6 cases the author has observed only nosebleed. Cutaneous purpuric manifestations have been lacking in the author's cases. Joint disturbances of some severity and cramp-like pains in the lower extremities are not uncommon. Dyspnea on exertion or even edema of the lower extremities may develop and cardiac insufficiency may produce symptoms most troublesome to the patient. Fever is absent.

The diagnosis can be made at sight with reasonable accuracy by one who has carefully observed a typical case previously. The face and ears exhibit a peculiar dusky redness seen in no other disease. It is furthermore quite distinct from ordinary cyanosis, however intensive, in that the red dominates the color field as far as the face is concerned. The extremities are markedly cyanotic. The depth and degree of the cyanosis is greatly intensified by exposure to cold and the dependent position. Decided enlargement of the spleen is present almost invariably and may attain large proportions. It is smooth, indurated and seldom or never fixed by adhesions.* All of the author's cases showed marked enlargement. The liver is usually decidedly enlarged.

Albumin and casts have been present in 6 cases occurring in the author's practice and in all the blood-pressure was distinctly high. In all cardiac hypertrophy and dilatation were manifest. Many cases are reported which have lacked circulatory disturbances of this nature; and, doubtless, a large number of the cases on record are unworthy of inclusion. It is certain, however, that the typical cyanosis with splenomegaly and erythrocytosis may exist without high blood-pressure. Internal hemorrhages and thromboses are common terminal events. Palsies of cranial nerves have occurred in two of the author's cases. Irregularities in the cutaneous sensibility are not rare and the deep reflexes may be asymmetrical.

THE BLOOD.—Hemoglobin values of 165 and even 220 (by Palmer's method) have been reported, but in one of Cabot's cases it was but 85 with a count of 8,484,000 reds and 15,000 whites, and in another 105 with a count of 11,352,000 reds. Moderate or absent leukocytosis is the rule. The highest erythrocyte count reported is 14,800,000 per cubic millimeter. The color index is low, the coagulation time variable and the behavior of the erythrocytes to salt solution is normal.

The specific gravity of the blood is high, that of the serum normal and the freezing point shows no abnormal variation. The blood volume is increased greatly and this is due to the increase of erythrocytes alone, the ratio of cells to plasma being nearly 75 to 25 in certain cases as compared with the normal ratio of 46.8 to 53.2. The oxygen capacity and avidity alike seem to be normal. The blood appears viscid and the depth of color is intensified. The blood smear appears normal but a critical examination may establish the presence of a certain amount of anisocytosis and polychromatophilia.

Blood-platelets may be increased, diminished, or normal in numbers.

If an increase of white cells is noted it will be found to be a polymorphonuclear increase. A few nucleated reds may be found in certain cases and the same may be said of the myelocytes. The excretion of bilirubin is such as to indicate that hemolysis is not diminished in this disease. The serum colloids and basal metabolism are normal or nearly so. The increased air intake obligatory in such cases adjusts the oxygen supply to the greater necessities of these patients and as might be anticipated the tissue need is satisfied without excess oxygen required by the circulation itself; hence the venous blood is abnormally rich in oxygen. In every case so far observed by the author the heart is enlarged and the circulation sluggish. It is affirmed by competent observers that the volume output from the heart is not increased.

---

* In a case hereafter referred to as under observation for three years past the primarily gigantic spleen is greatly shrunken and the liver has assumed almost a normal outline. The last blood count showed over 8,000,000 erythrocytes.

Clinical Varieties.—An attempt has been made to establish the occurrence of certain classifiable types of erythremia. The author believes it to be a futile and thankless effort. He had occasion a few years ago to review carefully all accessible literature and found that while certain variants doubtless occurred, almost without exception the cases entitled to a separate classification could be wiped off the list of proven erythremias. We have no knowledge of the time required for the development of this ailment but only deny a separate classification to cases developed in youth.

Treatment.—Splenectomy is not to be attempted. It is ineffective and unjustified from any and every viewpoint. The repeated **withdrawal of blood** has given great relief in the author's cases. Roentgenization and radium have not proven of any particular value in the author's experience. Benzol seems to exercise a beneficial effect upon the disease, but in the sole instance coming under personal observation in which it was used it produced an almost complete sexual impotence more harassing to the patient than the disease itself. This drug is supposed to inhibit or diminish marrow activity.

In general the treatment is wholly **symptomatic** and the greatest stress should be laid upon the adoption of a mode of life that will conserve the patient's slowly waning strength and a diet that will fill his nutritional needs without involving gastro-intestinal disturbances.

Prognosis.—Death usually results from some other cause than the disease itself. It is extremely slow and halting in its progress and, as stated previously, one cannot fix the date of its onset. It progresses by fits and starts; remissions may be long-enduring but these are only partial. The longest duration of life observed by the author personally in an established case is nine years from the time of his first visit. This patient is still living and able to attend to his business.

Pathology.—The bone marrow shows congestion, being deep red throughout, and bloody. The spleen is deeply engorged but structurally unchanged. All blood-vessels are injected.

BIBLIOGRAPHY

Hemophilia

ADDIS. Quart. Jour. Med., January, 1908. Proc. Soc. Exper. Biol. and Med., N. Y., 1916-17, xiv, 19. Quart. Jour. Med., Oxford, 1910, iv, 14. Jour. Path. and Bact., 1910-11, xv, 427.
ARNSPERGER. Deutsch. med. Wchnschr.; synop. in Arch. mal du coeur, January, 1911.
BARKER, L. F. Monographic Medicine, Vol. III, 237, D. Appleton & Co., New York.
BETTISON, D. L. Texas State Jour. Med., April, 1920, xv, 429.
BIENWALD, P. Deutsch. med. Wchnschr., 1897, xxvii, 28.
BIGELOW. Jour. A. M. A., July 30, 1910.
BOSANYI, A. V. Jahr. f. Kinderh., Berlin, 1919, n. F., xc, 1-26.

Broca, M. London Lancet, 1910, ii, 203.

Bucura, C. Ueber Hämophilie beim Weibe., Wien u. Leipzig, 1920, A. Holder.

Bullock, W., and Fields, P. Eugenics Lab. Memoirs, London, 1911, xii, 169.

Camac, C. N. B. Handb. Mtd. Sc., N. Y., 3rd Edition, 1915, v, 176.

Chalier, J. Rev. de Méd., Sept.-Oct., 1919, xxxvi, 522; abstr. Jour. A. M. A., March 20, 1920, lxxiv, 833.

Coca. Univ. Penn. Med. Bull., October, 1908.

Dorrance and Nate. Jour. A. M. A., August 13, 1910.

Duke. Jour. A. M. A., October 1, 1910.

Emilie-Weil, P. Bull. Acad de Méd., Paris, Nov. 25, 1919, lxxxii, 374; abstr. Jour. A. M. A., Jan. 31, 1920, lxxiv, 359.

Escudero, M. M. Cron. med.-quir. de la Habana, Jan., 1919, xlv, 16.

Etlinger, N. v. Jabhr. f. Kinderh., Leipzig, 1901, 3 F., iv, 24.

Feliciangeli, G. Policlinico (sez. prat.), Jan. 3, 1921, xxviii, 8.

Fleig. Soc. de Biol., July 6, 1907; synop. in Folia Hæmat., 1907, i.

Fonio, A. Mitt. a. d. Grenzgeb. d. Med. u. Chir., Jena, 1914, xxviii, 642.

Fry. N. Y. Acad. of Med., June 2, 1898.

Gangani. Synop. in Folia Hæmat., April, 1910.

Gilcreest, J. E. Texas Jour. Med., 1913, viii, 302.

Gocht, H. Verhandl. u. Deutsch. Gesellsch. f. Chir., Berlin, 1899, 359.

Grandidier, J. L. Die Hämophilie, oder die Blaterkrankheit. 2. neue Aufl., Leipzig., 1877, O. Wigand.

Greene. Medical Diagnosis, 4th Ed., p. 166, P. Blakiston's Son & Co., Phila., Pa.

Hahn. N. Y. Med. Record, October 8, 1910.

Hayden, A. A. Ann. Otol. Rhinol. and Laryngol., March, 1920, xxix, 37.

Henke. Arch. f. Laryngol. u. Rhinol., Berlin, 1919, xxxii, 89.

Hess, A. F. Johns Hopkins Hosp. Bull., 1915, xxvi, 372.

Hotz. Ztschr. f. Chir., April, 1910, civ.

Howell, W. H. Arch. Int. Med., 1914, xiii, 76. Amer. Jour. Physiol., Boston, 1912-13, xxxi, l. Harvey Lecture, Phil. and London, 1917, Series xii, 273.

Howell, W. H., and Holt. Amer. Jour. Physiol., Boston, 1918-19, xlvii, 328.

Hurwitz, S. H., and Lucas, W. P. Arch. Int. Med., 1916, xvii, 543.

Konig, F. Samml. klin. Vortr., Leipzig, 1891, Chirurgie No. 11, xxxvi, 233.

Labbe. Jour. Méd. Franç., 1910.

Lambert. Brit. Med. Jour., July 13, 1907.

Leary. Bost. Med. and Surg. Jour., July 16, 1908.

Litten, M. Hemorrhagic diseases. Nothnagel's System of Medicine, edited by A. Stengel, 1905.

Lommel. Zentralbl. f. inn. Med., 1908, xxvii, 28.

Lucas, W. P. Boston Med. and Surg. Jour., November 18, 1909.

Martin, C. F. *In* Forchheimer's Therapeusis of Internal Disease, Vol. III, 860, D. Appleton & Co., New York.

McLean, J. Oxford Medicine, Vol. II, 799. *Amer. Jour. Physiol., Boston, 1917, xliii, 586; and 1916, xli, 250.

Minot, G. R., and Lee, R. I. Arch. Int. Med., 1916, xviii, 474.

Morawitz, P., und Lossen, J. Deutsch. Arch. f. klin. Med., 1908, xciv, 110.

Mosenthal. Jour. A. M. A., 1910, i, 1913.

Nasse, C. F. Archiv d. med. Erfah. im. Gebiete der prak. Med. u. Staatsarzneikunde. hrsg. von Horn, Nasse und Henke. Berlin, 1920, May-June, p. 385.

Nobecourt, P. Paris Méd., Dec. 6, 1919, ix, 452; abstr. Jour. A. M. A., Jan. 24, 1920, lxxiv, 286.

Nobecourt, et Tixier. Soc. méd. des hôp. de Paris, October 22, 1910.

Nolf, P. Ergebn. d. inn. Med. u. Kinderh., Berlin, 1912, ix, 275.

Nolf et Herry. Rev. de Méd., Paris, 1909, xxix, 841.

Osler, Sir W. Practice of medicine, 8th Ed., p. 755, D. Appleton & Co., New York.

Otto, J. C. The Medical Repository, New York, 1903, Vol. VI, p. 1.

Pelissard, et Bonharnon. Presse méd., 1906, lxxvii; synop. in Folia Hæmat., 1907, i, 278.

Pepper, and Nisbett. Jour. A. M. A., xlix, 1907, 385.

Peterson, E. W. Arch. Pediatrics, N. Y., 1915, xxxii, 284.

Ranzier. Modern treatment of hemorrhages. Synop. in Arch. mal du coeur, September, 1910.

Rave, A. Beobachtungen u. Schlüsse aus der prak. Arzneiwissenshaft. Münster, 1796, ii, 12.

Renar. Arch. mal du coeur, February, 1911.

Rothschild, N. Ueber das Alter der Hæmophile. Inaug. Diss., München, 1882.

Rouchetti, V. Riforma med., Napoli, 1920, xxxvi, 719.
Roussot. Thèse de Lyon, 1910, 47, 1909–10.
Sahli. Ztschr. f. klin. Med., 1905, lvi, 264. Deutsch Arch. f. klin. Mediz., Leipzig, 1910, xcix, 518.
Salomoni. La Riforma Medica, 1900, 172, 254.
Sayer, J. H. Jour. A. M. A., 1912, lviii, 106.
Schelbe. Jahrb. f. Kinderh., October, 1908.
Schwartz and Ottenburg. Amer. Jour. Med. Sc., July, 1910.
Steiner, W. R. Johns Hopkins Hosp. Bull., 1900, xi, 44.
Vines, H. W. C. Quart. Jour. Med., April, 1920, xiii, 457.
Voncken, J. Jour. A. M. A., July 31, 1920, lxxv, 307.
Weil, P. E. Bull. Soc. Méd. des hôp. de Paris, October 26, 1906; also November 2, 1906. Presse Méd., October 18, 1905. Cong. Franç. de Méd., IXieme Session. Médécine, March, 1920, 1, 354; abstr. Jour. A. M. A., June 5, 1920, lxxiv, 1609.
Welch, J. E. Amer. Jour. Med. Sci., June, 1910.
Wright, Sir A. E. Brit. Med. Jour., 1893, ii, 223. *In* Allbutt and Rolleston's System of Medicine, London, 1909, Vol. V, 918.

Purpura

Barker, L. F. Monographic medicine, Vol. III, 239, D. Appleton & Co., New York.
Bensaude, R., and Rivet, L. Arch. gen. de méd., 1905, i, 193 and 272.
Billings, J. S., Jr. Johns Hopkins Hosp. Bull., 1894, v, 65.
Chestnutt, J. Jour. Arkansas Med. Soc., Little Rock, 1914–15, xi, 215.
Christian, H. A. Oxford medicine, Vol. II, 779. Jour. A. M. A., 1917, lxix, 325.
DeLange, C. Nederlandsch Tijdschr. v. Geneesk., May 3, 1919, li, 1564; abstr. Jour. A. M. A., August 16, 1919, lxxiii, 568.
Denys, J. La Cellule, 1887, iii, 445.
Duke, W. W. Jour. Exper. Med., 1911, xiv, 265. Jour. A. M. A., 1910, lv, 1185. Arch. Int. Med., 1912, x, 445.
Elliott, C. A. Arch. Int. Med., 1909, iii, 193.
Elliott, E. A. Med. Jour. Australia, Feb. 28, 1920, i, 191.
Frank, E. Berlin. klin. Wchnschr., 1915, lii, 454.
Gougerot, H., et Sabin, H. Arch. d. mal du coeur, Paris, 1911, iv, 86.
Greene, C. L. Medical diagnosis, 4th Ed., p. 164, P. Blakiston's Son & Co., Phila., Pa.
Harris, T. J. N. Y. Med. Jour., August 23, 1919, cx, 311.
Henoch, E. Berlin. klin. Wchnschr., 1874, xi, 641.
Johannessen, C. Norsk. Mag. f. Lægevidensk., Dec., 1918, lxxv, 1336; abstr. Jour. A. M. A., March 8, 1919, lxxii, 768. Norsk. Mag. f. Lægevidensk., Nov., 1918, lxxix, 1209; abstr. Jour. A. M. A., Jan. 25, 1919, lxxii, 318.
Ledingham, J. C. G. Lancet, London, 1914, i, 1673.
Ledingham, J. C. G., and Bedson, S. P. Lancet, London, 1915, i, 311.
Lee, R. I., and Robertson, O. H. Jour. Med. Research, 1916, xxxiii, 323.
Le Sourd, L., et Pagniez, P. Jour. de physiol. et de path. gén., 1911, xiii, 56.
Levin, J. J. Med. Jour. So. Africa, January, 1920, xv, 135.
Litten, M. Hemorrhagic diseases. Nothnagel's System of Medicine, edited by A. Stengel, 1905.
Lucas, W. P. Boston Med. and Surg. Jour., November 18, 1909.
Mann, W. L., Jr. U. S. Nav. M. Bull., Washington, 1915, ix, 438.
Martin, C. F. *In* Forchheimer's Therapeusis of Internal Diseases, Vol. III, 858, D. Appleton & Co., New York.
Matthews, and Carpenter. Amer. Jour. Med. Sci., July, 1911.
Minot, G. R. Amer. Jour. Med. Sci., 1916, clii, 48. Arch. Int. Med., 1917, xix, 1062.
Moffatt, C. F. Canad. M. A. Jour., May, 1920, x, 452.
Moreira, A. E. Semana Méd., July 31, 1919, xxvi, 125.
Nobecourt, P., et Mathieu, R. Paris Méd., Dec. 4, 1920, x, 412; abstr. Jour. A. M. A., Feb. 5, 1921, lxxvi, 411. Arch. de méd. d. enf., Dec., 1920, xxiii, 689; abstr. Jour. A. M. A., Jan. 29, 1921, lxxvi, 341.
Osler, Sir W. Practice of medicine, 8th Ed., p. 750, D. Appleton & Co., New York. Amer. Jour. Med. Sci., 1893, cx, 629; 1904, cxxviii, 1 and 751. Brit. Jour. Dermat., 1900, xii, 227. Brit. Med. Jour., 1914, i, 517.
Pratt, J. H. In Osler & McCrae's Modern Medicine, Vol. IV, p. 694, 1915, D. Appleton & Co., New York. ;
Reh, T. Arch. de méd. d. enf., March, 1920, xxiii, 179; abstr., Jour. A. M. A., May 8, 1920, lxxiv, 1354.

Roubier, C., et Brette, P. Progrès méd., Dec. 6, 1919, xxxiv, 488; abstr. Jour. A. M. A., Jan. 24, 1920, lxxiv, 287.

Roubier, C., et Richard. Arch. d. mal du Coeur, Oct., 1920, xiii, 448; abstr. Jour. A. M. A., Feb. 12, 1921, lxxvi, 480.

Selling, L. Bull. Johns Hopkins Hospital, 1910, xxi, 33.

Steiger, P. Wien. klin. Wchnschr., 1913, xxvi, 1749.

Stevens, A. R., and Peters, J. P., Jr. Jour. Urology, Feb., 1920, iv, 1.

Stokes, J. H. Amer. Jour. Med. Sci., Feb., 1919, clvii, 157.

Strack, G. Amer. Med., Burlington, Vt., and N. Y., 1915, n. s. x, 297.

Taylor, J. G. Clin. Jour., London, 1913–14, xlii, 542.

Thrash, E. C. Jour. M. A. Georgia, Feb., 1920, ix, 62.

Watabiki, T. Sei-i-Kwai Med. Jour., 1918, xxxvii, 47.

Weil, P. E. Comptes Rendus de la Soc. de Biol., December 8, 1906. Trib. méd., Jan. 12, 1907. International Clinics, xvii, 1907. Trib. méd., 1907.

Weil, G. C., and McMeans, J. W. Jour. Infect. Diseases, Chicago, 1914, xv, 151.

Wright, J. H. Jour. Morphol., 1910, xxi, 263.

Polycythemia

Anders, J. M. Amer. Jour. Med. Sc., 1907, cxxiii, 829.

Barker, L. F. Monographic medicine, Vol. III, 204, D. Appleton & Co., New York.

Bergmann, G. von, and Plesch, J. München. med. Wchnschr., 1911, lviii, 1849.

Bing, H. I. Ugesk. f. Læger., March 11, 1920, lxxxii, 337; abstr. Jour., A. M. A., May, 15, 1920, lxxiv, 1432.

Blumenthal, R. Arch. de méd. Expér. et d'Anat. Pathol., 1907, xix, 697.

Bock and Means. Unpublished article.

Bottner, A. Deutsch. med. Wchnschr., Jan. 15, 1920, xlvi, 66; abstr. Jour. A. M. A., June 25, 1920, lxxiv, 1804.

Boycott, A. E., and Douglas, C. G. Jour. Path. and Bact., Cambridge, 1909, xiii, p. 117.

Collins. Medical Record, November 21, 1903.

Engelking, E. Deutsch. med. Wchnschr., Oct. 7, 1920, xlvi, 1140.

Geisbock, F. Deutsch. Arch. f. klin. Med., 1905, lxxxiii, 363.

Gitlow, S. Medical Record, Feb. 5, 1921, xcix, 227.

Goyena, and Masoch. Abstracted in Jour. A. M. A., Nov. 29, 1919.

Greene, C. L. Medical diagnosis, 4th Ed., p. 159, P. Blakiston's Son & Co., Phila., Pa.

Haldane, J., and Smith, J. L. Jour. Physiol., 1900, xxv, 331. Brit. Med. Jour., 1919, ii, 65.

Herrnheiser, G. Deutsch. Arch. f. klin. Med., Oct., 1919, cxxx, 315; abstr. Jour. A. M. A., May 29, 1920, lxxiv, 1549.

Hurter. Deutsch. Arch. f. klin. Med., 1912, cviii, 1.

Hurwitz, S. H., and Falconer, E. H. Jour. A. M. A., 1918, lxx, 1143.

Keith, N. M., and others. Arch. Int. Med., 1915, xvi, 547.

Koster, G. München, med. Wchnschr., 1906, liii, 1056.

Lamson, P. D. Jour. Pharm. and Exper. Therap., 1915–16, vii, 169; abstr. in Jour. A. M. A., Oct. 30, 1920, lxxv, 1228.

Lommel, F. Deutsch. Arch. f. klin. Med., Leipzig, 1906, lxxxvii, 315; also 1908, xcii, 83.

Lucas, W. S. Arch. Int. Med., 1912, x, 597.

Lundsgaard, C. Jour. Biol. Chem., 1918, xxxiii, 133. Jour. Exper. Med., 1918, xxvii, 179, 199, 219.

Lutembacher, R. L'Erythremie, Paris, 1912, No. 316 (Thèse de Paris).

McLester, J. S. Jour. Amer. Med. Assoc., 1914, lxii, 1381.

Malassez. Compt. rend. Soc. de biol., 1872, xxiv, 236.

Martin, C. F. *In* Forchheimer's Therapeusis of Internal Diseases, Vol. III, 877, D. Appleton & Co., New York.

Means, J. H., and Newburgh, L. H. Trans. Assoc. Amer. Phys., 1915, xxx, 51.

Monro, T. K. Lancet, London, 1913, i, 1015.

Morris, R. S. Johns Hopkins Hosp. Bull., 1910, xxi, 37.

Naunyn. Korrespond. f. Schweizer Aerzte, 1872, ii, 300.

Orlowski, W. Progrès méd., 1912, 10, 117.

Osler. Osler's Practice of medicine, 8th Ed., 1917, p. 757, D. Appleton & Co., New York. Johns Hopkins Hosp. Bull., 1903, xiv, 91. American Jour. Med. Sciences, 1903, n.. s. cxxvi, 187. British Med. Jour., Oct. 17, 1908; also 1904, i, 121.

Palmer, W. W. Jour. Biol. Chem., 1918, xxxii, 119.

Parkinson, J. Lancet, London, 1912, ii, 1425.

Preis. Synop. in Folia Hæmat., 1904, i, 425.

Rendu and Widal. Bull. et mém. Soc. méd. d. hôp. de Paris, 1899, c s., iii, 528.

Rosin, H. Therap. Rundschau, 1908, ii, 677.

Rover, F. München. med. Wchnschr., 1911, lviii, 2791.

Senator, H. Polyzythämie und Plethora. Berlin, 1911, A. Hirschwald.

Stadie, W. C. Jour. Exper. Med., 1919, xxx, 215.

Turk, W. Wien. klin. Wchnschr., 1904, xvii, 153; synop. in Folia Hæmat., 1904, 425. Wien. klin. Wchnschr., 1902, 163 and 372.

Vaquez. Soc. de Biol., 7 Mai, 1892; also 2 Mars, 1895. Bull. et mém. Soc. méd. d. hôp. de Paris, 1895, 3 s., xii, 60. Compt. rend. Soc. de biol., Paris, 1895, 10 s., ii, 142. Bull. méd., Paris, 1892, vi, 849. Compt. rend. Soc. de biol., 1892, xliv, 384.

Vaquez, H., et Laubry, C. Bull. et mém. Soc. méd. d. hôp. de Paris, 1904, 3 s., xxi, 880.

Viault. Compt. rend. Acad. d. sc., 1890, cxi, 918.

Vogel, J. Virchow's Handb. der spez. Path. u. Therapie, 1854, i, 377.

Ward, G. R. Proc. Roy. Soc. Med., London. 1913, vi, 83.

Weber, F. P. Folia Hæmat., Leipzig, 1908, v, 701. In Allbutt and Rolleston's System of medicine, London, 1909, Vol. V, 831. Lancet, London, 1913, i, 1307. Quart. Jour. Med., 1909, ii, 85.

Weber, F. P., and Watson, J. H. International Clinics, Philadelphia, 1905, 14th Ser., iv, 47.

Winter, K. Med. Klin. 1908, ii, 1017.

IMPORTANT

THE CONTENTS OF THIS AND ALL OTHER VOLUMES ARE INDEXED IN THE SEPARATELY BOUND DESK INDEX.

The subject you are looking up may be closely allied with another and by using the Desk Index of all ten volumes it obviates the necessity of searching through several individual indexes thus saving your time.